Are Markush Structures Matters of Chemistry and Law or Just Figments of the Imagination?*

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Markush disclosures caused problems for both database producers and users. Also there was the necessity for such claims expressed by the patent attorneys, especially in the pharmaceutical area. The authors of this paper looked at this problem paying particular attention to the requirements of patent law and to the needs of chemistry as a science. Account is taken of the views expressed in previous publications in the area. It is argued that the so-called “nasties” and “super-nasties” arise because the basic principles of science and of patent law are being ignored.

Introduction

When one looks at the reports of the 'Roundtable' discussion one becomes aware that the participants see the application of patent law to Markush claims in two opposing ways. Although generic formulas which occur in chemical patents are referred to as Markush formulas, the original Markush patent (US 1506316, 1924) did not contain a generic formula in the claims. It claimed a process for the manufacture of dyes which comprised coupling with a halogen-substituted pyrazalone, a diazotised unsulphonated material selected from the group consisting of aniline, homologues of aniline, and halogen substitution products of aniline, the product being capable of dyeing silk and wool in an acidulated bath.

According to the Manual of Patent Examining Procedure [Washington DC (1961)] it is stated that (in the sphere of chemistry after a ruling in 1925 on the Markush doctrine) it was permitted, in the absence of a suitable commonly accepted generic expression commensurate in scope, to enumerate the different species that are to be grouped together into a genus. Such enumeration was

permitted for both process (method) and composition claims.

As far as later decisions are concerned, the Markush patent does not provide support for those cases where the characterisation of claimed products relies solely on their method of preparation. The pyrazalene dyes in the Markush patent could be represented by a structural formula. Consequently, the Markush structures found in patent law, in spite of the name, cannot be based on the Markush decision.

On the other hand, not only do Markush structures often not correspond to specific chemical compounds but many do not even characterise a type of compound which, in one author’s opinion could form the basis of an invention.

In such cases, neither the normally skilled person nor even the very highly skilled organic chemist could clearly envisage all the compounds covered by the Markush structure. It is practically impossible to retrieve all the relevant compounds in a prior art search under normal circumstances without having to deal with the “nasties” and “super-nasties”.

Apparently, the absence of a suitable resolution to the problem caused some of the participants at the Round-table to suggest a solution which conflicts with the fundamental tenets of organic chemistry, namely to describe a chemical compound without using its chemical formula!

Is there an alternative to structural formulas?

Surprisingly, some of the participants at the Round-table believed that there may be alternatives to the use of structural formulas. Thus, Dr Stone suggested that the structural formula could be replaced with functional terminology. He stated “Markush practice, dating back to Eugene Markush, was employed in order to define chemically something which was difficult to establish in otherwise generic terminology. But, as the USPTO is beginning to accept an additive, let’s say, as a retentive polymer to a specific surface, the need for a Markush group actually diminishes. Therefore, the Markush group can be put into Claims 2 or 3 and the attorney who is writing the claims no longer needs to try to define a Markush group. This is because he is able to establish in good meaningful functional terminology a generic claim that can be backed up with somewhat narrower...”

When one looks at a claim for new chemical structures (chemical compounds), no patent attorney is able to establish the structure purely in words, even if it were permitted. The claim for a chemical compound must include information about the chemical structure. The example quoted by Dr Stone (with the polymer) really has nothing to do with the problem under consideration. This is because organic chemists visualise compounds in terms of their formula. The structure of a chemical represents a statement of the chemical properties of the compound and gives guidance on the order of chemical bonding in the molecule.

In effect, the suggestion of Dr Stone to substitute the generic structure formula by “meaningful functional terminology” represents a step backward from structural chemistry to the pre-structural period, about which Werler had written in a letter to Bercelius “Now organic chemistry can drive everybody mad. I see it as a wood full of wondrous things, but it is an impenetrable thicket without an outlet, into which you would not dare to go.”
While Dr Stone would have us return to prestructural chemistry. Dr Brown suggests that we take a quantum leap away from structural formulas. She believes that the “practising scientist’s aim must be to find more sophisticated ways of describing molecules. For example, molecules could be described in terms of their electron cloud conformations and densities and from that, deduce their biological activity.

Research in the sphere of quantum chemistry has shown that a molecule is a quantum mechanical system of nuclei and electrons. The quantum theory removes the partition between a subject and a process, that is, it explains reactability, but it does not replace the need for the structural chemistry in the description of a chemical compound. What is more, it has been shown that while the use of structural analogy when deciding on the presence and position of biologically active groups led to the synthesis of effective fungicides, the application of analogies at the level of electronic structures was not successful.

The application of physics to chemistry was studied by Parton in 1959 and concluded “no scientific generalization based simply on a number of observations, even given the exact mathematical formulations, was as successful as the group of ideas which we call structural theory.”

Graphic formulas of organic chemistry are more significant to the chemist than any theory about atomic arrangements. The structure is a wonderfully practical method of representing the huge variety of chemical compounds. Even the picture of one double bond in ethylene represented as a general electron cloud is an extremely complicated drawing. In order to represent the many different molecules in this way would require a Malevich. Even if there was one set of simple visual symbols available to all chemists throughout the world, patent systems would still be in difficulties.

One way out would be to follow the rules of organic chemistry. It was said by Fuchs, not without foundation, that “subjects concerning the field of chemistry can only be adequately described by chemist.” At the beginning of the 19th C, Bereelius warned “in science, the time is coming when chemists, who possess highly limited aptitudes but who yearn for fame, will abuse the system by publishing conclusions based on the results of badly carried out experiments, filling organic chemistry with false data”. But, could even this great Swedish chemist have imagined the problems being caused at the end of the 20th C by the “paper” chemistry published under the aegis of patent law? “Paper” chemistry refers to those compounds claimed in specifications which have never been made or characterised but which are treated as being real.

This “paper” chemistry degrades science and discredits the patent system. The information scientists may be able to continuously improve their retrieval systems but this will not change the situation.

Are Markush structures really chemical structures?

In our opinion, one of the causes of the problems with Markush structures is the disregard for the position indicated above which suggested that chemistry can only be described adequately by chemists.

No chemist would dare to describe the compounds of US 4737184 by the formula:

$$\text{JSO}_2\text{NHC(W)N(R)A}$$

or those of US 4838925 by the formula:
L - S(O)₂N(R) - C(W) - A or
L - S(O)₂N = C(G) - A,        ... (2)
as reported by J Sibley,⁶ or those of EP
314239 as:
A — B — E — G — J,        ... (3)
reported by Norton.⁶ In fact, such formulas
cannot realistically be described as generic
chemical structures because they carry little
or no chemical information.

In general, nobody is against broad claims
but the degree of generalization must be
limited by the application of legal and tech­
nical criteria. If the generic structures given
cannot be recognised as chemical formulas
by scientists then the patent law is already in
trouble. If the various alternative specific
sub-structures on which such claims are
based can only be enumerated by the use of
several pages of text, then such specifica­
tions may fairly be called “gibberish”.

Bearing such claims in mind, it is impossible
to agree with Dr Jenny¹ that “since the hu­
man brain is able to register generic/spe­
cific or generic/subgeneric connections fairly quickly, it can detect quite speedily
whether a compound or type of compound
falls under a generic formula.”

One has only to look at US 4838925 cited by
J Sibley,⁶ to be convinced of the limited possi­
bilities of the human brain in this area. The
situation is complicated enough when there
are just a few of these patents and becomes
almost insurmountable when relevant docu­
ments must be retrieved.

It is quite evident that such documents
which do not contain chemical structures
should not be allowed to reach the prelimi­
nary examination stage. The formal reasons
for rejecting such documents already exist
in the regulations of all the patent offices. For
example, in accordance with the PCT, “The
formula must be clear and exact and the
degree of generalization must not exceed
what is reasonable”.

The Markush structures which cannot be
fully classified as a whole in accordance with
the IPC and which include no chemical in­
formation, should be rejected on formal
grounds at the preliminary examination
stage. However, our searches show that
such non-chemical structures comprise no
more than 6% of classes C07 and C08. How­
ever, all Markush structures which give only
partial information about their chemical na­
ture should also be suppressed.

For example, the claim of DE 3446778 dis­
closes new imidazole derivatives of formula
(4) for use as pharmaceuticals.

The structures embraced include imida­
zopirimidines, imidazopiridazines and imi­
dazotriazines all optionally substituted by
sulphur-containing groups such as mercapto- and sulphonyl-groups, whilst R can be
a sulphamide group.

The specification has been classified in two
parts of the IPC: C07D 487/04 and A61K
31/44, C07D 487/04 indicates heterocyclic
condensed systems containing only nitro­
gen as ring heteroatoms. It is difficult to fault
this in so far as all the optional condensed
cycles condensed with imidazole fall
within one general grouping of the IPC, that
is, the classification assigned deals only in a
non-specific way with one essential element
of the chemical structure.

We can compare this with the disclosure in
another document of what is essentially a
different structure but which can also be constructed as covering some of the structures claimed above. Thus, EP 0261004 describes imidazoles of the formula (5):

$$D \rightarrow L$$

Where D can be alkyl, or phenyl.

G can be alkyl, alkoxy, alkylthio, alkylsulphonyl, or D and G together can form the groups:

This document was classified in the same way as DE 3446778 with the IPC C07D 487/04 in spite of the fact that most of the specific structures were outside the definition of this code being either uncondensed imidazoles (C07D 233/00) or were condensed with carbocycles, that is, benzimidazoles (C07D 235/00).

This example shows quite convincingly how:

- the same compounds can be represented by very different generic structures; and
- the same type of generic structure can embrace quite different types of specific compounds.

These qualities are not inherent in true chemical structures in so far as these structures reflect the “physiognomy” of the chemical compound and must show the number and type of the atoms present and the nature of the bonds between them in sufficient detail that this “physiognomy” is comprehensible.

It is proposed that such requirements, which are in accordance with the postulates of chemistry, should become part of patent law with regard to generic structures in so far as the chemical structures are the subject of the invention.

Some authors have suggested that the type of chemical compound should be the subject of the invention. Thus, Jenny maintained that “To the researcher in the field of chemistry it is the type of the compound that is of primary importance and not the sum of the individual compounds that fall under it.” This assumes that the type of compound is reflected by the generic structure.

Milne mentioned a proposal that emerged from the Round-table discussion which was that “The structural part of a compound that underlies the property that is claimed should be specified precisely, but all non-essential appendages — alkyl groups and the like — should be replaced by either ‘anything’ or ‘etcetera’. In his opinion “such frank type II Markush formulations would simplify both examination and indexing, as well as writing.”

Essentially, both authors propose claims to the type of chemical compound but not to the totality of all the specific compounds. Such a suggestion is unsuitable because of objections which have their origin in the underlying chemistry. The problem lies in the field of organic chemistry, where there is a great stock of knowledge and experimental data concerning the inter-relationships between chemical compounds and their known practical properties.

For example, as early as 1936, Shrader proposed that organic compounds of phospho-
rus of the general formula (7) would be biologically active provided:

- \(R_1R_2P(O\text{ or }S)\text{Acyl};\)  \(\ldots\) (7)
- the oxygen or sulphur atom was bound directly to the five valent phosphorus atom;
- \(R_1\) and \(R_2\) may be alkyl, alkoxy, alkylamino, heteroalkyl, etc.; and
- acyl is the residue of an organic or inorganic acid.

Despite this disclosure, for almost 60 years, all countries have been accepting patents directed towards novel compounds which fall within the scope of the general formula given above. The truth of this may be confirmed simply by looking at the number of patents within the IPC class C07F. If we followed the suggestion of the authors, anybody subsequently trying to claim the same type of compound in which \(R_1\) and \(R_2\) are “anything” would have had their applications disallowed and work within the area would have stopped.

There is a tendency to think that the ‘Markush’ problem is restricted to organic chemistry but this is not true; the same situation is found with dyes, etc. Herbicides and pharmaceuticals of the sulphonamide type \(\text{[A. McKready, Patent Office Practice, pp 85, 93, ch. XI. Williams Co, NY (1954)]}\) have also been patented very widely over the last 10 years.

The formal requirements of patent law are known and they do not allow such claims. “The formulas in patents are often disallowed by the Appellation Courts on the grounds of their excessively broad claims, with statements to the effect of: ‘the formula would prevent further progress in this area’. The claims are broader than the disclosed invention or, ‘the claims are unacceptable because the formula employs indefinite alternative groups’. However, it is not just a matter of the requirements of the patent law, it is also that the chemistry involved is characterized in the claims in a way which is not comprehensible to chemists.

**Markush structures; the doctrine of equivalents and unity of invention**

Two opposing opinions were voiced at the Round-table about the correlation of Markush structures with the doctrine of equivalents. John Terapane stated “The Markush claims almost by definition contain compounds that are disparate but not necessarily equivalent.” However John Brennan said “A Markush formula says that we are dealing with a group of functionally equivalent structures.” Such opposing views about a single aspect of patent law cannot be allowed to pass without discussion.

It is difficult to decide what definition of Markush structures John Terapane has in mind. According to the Manual of Patent Examining Procedure already mentioned a Markush claim is one in which, in the absence of a suitable commonly accepted generic expression commensurate in scope with the monopoly desired, the applicant enumerates the different species that are to be grouped together into a genus. The individual compounds possess at least one property in common which is mainly responsible for their function in the claimed relationship; it is clear from their very nature or from prior art that all of them possess this property. Quite evidently this means that all the compounds within the Markush formula must be functional equivalents.

In the literature, Markush structures are thought of as “generic chemical structures,
which contain one or more structural variations which are defined by the enumeration of alternatives."

It is known that, in accordance with the principle of unity of invention, a claim may include such alternative inventive features that are functionally equivalent and so, in accordance with this, it is acceptable that Markush structures include functional equivalents. The question remains — do the Markush claims found in patents really include only functional equivalents?

Before discussing this, it is worth noting that Norman Schmuff posed the question "To what extent does the doctrine of equivalents make broad Markush claims redundant in granted patents? If you can make a narrow claim and the doctrine of equivalents allow your coverage really to extend beyond your narrow particular claim to anything that is accomplished in substantially the same way, etc. etc. then isn't narrow claim just as good as one of these broad Markush claims?"  

Our answer must be quite unequivocal — in the case of chemical compounds, the doctrine of equivalents does not allow the broad interpretation found in patent claims. It is just this which, in our opinion, gives rise to these very broad claims.

The doctrine of equivalents is used mainly in the US courts to determine the monopoly rights of a patent. In effect it states that at least one of a combination of technical features may be replaced with an equivalent one provided the method and result are unchanged. But two important points must be emphasized:

- the scope of the doctrine of equivalents depends on the prior art that was available at the time the specification was written; and
- it must not be only unique feature.

A novel chemical compound is characterized by a unique feature, its structural formula. The generic formula (Markush structure) is a combination of all the unique individual compounds but not a combination of features of one subject.

The patenting of one chemical compound cannot stop the use of even analogous compounds produced later for the same purpose, provided they are different and they were not known before the date of the first patent.

The impossibility of using the doctrine of equivalents to increase the scope of patents for novel compounds to embrace analogous compounds can be demonstrated easily using a concrete example. In US 4838925 cited by J F Sibley, sulphonamides of general formula:

\[ L - \text{SO}_2 - NR - C(=W) - A \]  

are claimed as herbicides. The many claimed individual heterocyclic moieties that can be used as L, as a substituent of L, and as A, together with their optional substituents are set out and cover several pages of the specification.

Now, if we can imagine that this US patent, in fact claimed only one of the compounds listed namely, a compound of formula (9):

\[ \text{[Diagram of Compound (9)]} \]

Then later, somebody claimed the use, as herbicide, of a compound of formula (10):

\[ \text{[Diagram of Compound (10)]} \]
As the law stands at present, this later compound and its application as a herbicide would not be held to infringe the patent claimings. But, if the doctrine of equivalents were to be applied, then it could be argued that the use of compound does infringe and all kinds of insoluble difficulties would arise which would make patenting very problematical.

In fact, there are masses of earlier patents on sulphonamide herbicides and these would increase the difficulties still further. The first of these, if well drafted, would not only have prevented the patenting of US 4838925, but stopped all subsequent work in this field. This situation would arise in all areas of chemistry.

In practice, there are very many patents in class 71-92 of The US National Patent Classification all claiming sulphonyl urea type herbicides of general formula:

L — SO₂ — NH — C(=W) — NRA .... (11)

In addition, many of them claim almost identical compounds in which A is a triazine moiety and L is an optionally substituted benzene, naphthalene, furan or thiophene moiety. Several of these are illustrated in Table 1.

As can be seen, the compounds claimed are all of one type and we hold the same view as Jenny that the publication of the earliest patent in this series would have been an obstacle to the later patenting of the other patents.

The distinction between the various disclosures in Table 1 lies in the substituents, that is in the specific compounds and not in the type of compound, and it is the multiplicity of these compounds which is the main cause of the difficulties that arise when indexing for inclusion in databases.

If the substituents were not specific but were represented as 'anything' or 'etc etera' as proposed by Milne, then all patenting activity in the sulphonylurea area would have ceased after publication of the first patent with a description of such compounds. All the cited facts and arguments, in our opinion, show convincingly that the doctrine of equivalents cannot be used to enable a narrowly drafted claim to be subsequently broadened out. However, the doctrine of equivalents can be used during patent examination to reduce the scope of very broad Markush structures.

Markush structures involve a group of chemical compounds which, as the subject of an invention, according to the principle of unity of invention, must be technically equivalent. This equivalence of all members of the group may be determined by experiment or by structural analogy.

Where the Markush structure embraces a great number of structurally different compounds and the claims are supported by only a few specific examples, the application of the principle of unity of invention will allow one to formulate a correlation between them on the basis of the doctrine of equivalents.

However, this will require an agreement on the concept of 'nearest chemical structures' or structural analogues without which it is impossible to resolve the major difficulties in the patenting of chemical compounds.

**Is reduction to practice required when patenting chemical compounds?**

Here, there are also two opposing views on this question. On one hand, John Terapane suggests that: "The word ‘invention’ in the Patent Office (USPTO) and in patent law does not mean actual reduction to practice.
There is absolutely no requirement for even one example in a patent application. You can write a perfectly valid application without any examples... the execution of the patent application is constructive reduction to practice. This means that, in some instances, you don’t even have to build your device or make your compound if you firmly believe that it is going to work and there is nobody who can argue against you. So, (the word) ‘invention’ does not mean, as I think you are using it, actually making something, at least in US patent law.

Similarly, Paul Ginsburg, when discussing paper examples stated: “I think it is a well-established principle of US law that the value
or originality of an invention does not depend on how the invention was made." He goes on to say that the only criterion is "is it obvious in the light of the prior art or isn't it."\(^6\)

On the other hand, the opinion of the examiner Edward Miller is that "unless there is an example where the guy actually made it and set forth all the specific variables, R groups, X groups, whatever kind of groups there are, the patent is essentially worthless to us as basis for examination or as a means of wiping out a patent that was, in fact, granted."\(^6\)

The statements of Terapane and Ginsburg seem to contradict The Patent Office rules which say that the claims should reflect no more or no less than the subject of the invention which has been specifically characterized and which can be made without resorting to guesswork and supposition. If the claim is broader than the disclosures made by the applicant, the application must be rejected [A McKready, \textit{Practice of The Patent Office}, pp 77, ch XI. Williams Co, NY (1954)].

Let us consider the expression "The subject has been specifically characterized": in truth, if a device has been described by way of a drawing or like method, it is enough for one to judge whether or not it is workable. One device may be distinguished from another by its drawing and by the accompanying text. A chemical compound is described unambiguously in claims by a structural formula which is a simple symbol. But the existence of the structural formula alone does not establish either the method of making the compound or whether the compound even exists.

In order to prove that the compound really exists, the structural formula must be accompanied by additional information by which it can be identified such as its physical properties and method of manufacture. A chemist does not believe that a chemical compound exists unless its physical properties have been given. These properties can only be determined by means of research on the actual compound. That is why, during the 1960s, lawyers considered that, in line with the principles of organic chemistry, the subject as a whole was the compound together with its properties, and not just the formula.\(^9\)

If lawyers now think that it is permissible to claim chemical compounds without citing even one example, or to claim 2-3 million compounds on the basis of just one or two examples, then they must admit that it is possible to patent a formula which does not have a chemical foundation. This flies in the face of the basic principles of both chemistry and patent law because chemists do not want "paper" chemistry but patents that disclose real chemical compounds rather than graphic images of imaginary molecules. Putting aside the earlier precepts seems to be putting the cart before the horse.

The requirement for adequate experimental data to support the breadth of claims could provide one way for controlling the complexity of Markush structures. Of course it is not possible to get total control, but some limitation should be obtainable. The claims could be extended beyond the specific compounds supported by experimental data but only to those with closely analogous structures where there is a real probability of obtaining identical functional activity from a chemical point of view.
Novelty is an unworkable criterion for chemical compounds today

Novelty is one of the fundamental criteria of patentability but it can now be stated quite definitely that this criterion is not being fulfilled with regard to chemical compounds.

Earlier authors have already commented about this: for example, "The cost of retrieval and storage is rising continuously and the problems are compounded when dealing with patent information due to the complexity. No single examiner can carry out a search to meet the legal requirements in any country." Similarly: "Very complex Markush formulae are hard to understand and it takes considerable time and effort to prepare the input for a Markush database. Errors can occur in the processing; broad searches can lead to large number of false drops, the database can become too expensive and unwieldy." As a result, databases become unattractive for most searchers. But the problem is not so much inaccessible as the difficulty in unravelling the complex, tangled generic structures.

Justifiably, Norton maintains "The danger is that in the not too distant future, I can see the day when every patent which goes into the patent office will have prior art or overlap with the prior art in one of these types of patents and this will bring the whole patent system into disrepute." This still leaves the problem of carrying out the novelty search for a specific compound falling within the scope of the Markush structure claimed; but, if we apply the doctrine of equivalents, this is not strictly necessary. It is quite enough to find near known analogues with the same functional activity and to refuse the application on the grounds of obviousness.

Markush structures and "Selection invention"

Another way out of the difficulties arising from broad Markush structures was considered. In answer to Norton's remark, that the danger of broad claims which are not supported by experimental evidence was that they may inhibit somebody actually making one or more of the compounds later and that the products may have an entirely different useful activity, John Brennan made the following statement. "Peter was expressing, that perfectly good compounds in the future will be lost because of unduly broad claims at present. I think it is almost impossible to imagine how that would happen. I think the normal practice is to make the compound first and then see afterwards to what degree they are protected. Now, if the new compound has the same activity as was claimed in the past and to the same level, then you are not making any great contribution to the prior art. It is just something that does the job as well. If it has greater activity, you can make an invention of selection... So, these very broad claims for millions or infinite number of compounds are not, in the end,
going to damage a good invention that will come later on."

If in practice, it was possible to make compounds, define their activity and then be able to make a complete search to establish novelty or not, there would have been no need to hold the Round-table discussion in the first place. The problems caused by Markush structures would not exist. However, in reality, we all know that the difficulties do exist.

Norton's opinion is founded on actual practice which makes it possible to obtain patent protection for compounds which have never been made. Additionally, the inventor of a patent of selection is in a considerably worse situation to that of the inventor of a "super-nasty":

- the inventor must make the new compound or compounds in order to define the activity and to compare this activity with that of known compounds;
- the inventor must carry out a thorough search for novelty and be especially aware of the possible existence of "super-nastics" which will have to be found and comprehended in order to establish whether his compounds are new. We are presently discussing the hopelessness of this task; and
- the inventor must carry out research to ensure that the compounds have not been reported to have different activities.

The inventors of "super-nastics" have obtained a monopoly over an infinite number of compounds without the high costs of research, manufacture or testing. This is clearly inequitable. Why should somebody do all that is necessary to obtain a patent of selection when it is possible to claim "gibberish" without difficulty.

The criterion of "unobviousness" is an obstacle to unclear and excessive claims

After the 145th Meeting of The American Chemical Society in 1964, a collection of articles was published dedicated to patent problems in chemistry. In one of these, it was noted that "there is no area of patent prosecution in which rejection on the grounds of 'obviousness' has occurred more frequently than that of homologues or 'near analogues' of known compounds."" 

What are the principles on which such decisions are made? The answer can be found in another of the articles where it is stated: "The broad concept of homology between next-adjacent organic compounds is well known to every chemist. Making another novel compound which differs only by close homology, isomerism, replacing oxygen by sulphur or by double bond shift, is just an exercise in manipulative chemical procedures unless such obvious differences produce a physical thing of unexpected usefulness." In accordance with article 35, 103 of US Patent Law, "The subject matter as a whole must be unobvious", but in the case of chemical compounds "The subject matter as a whole" is not the structural formula but the physical material and its attendant properties.

Laurence notes "that the graphic formula, chemical nomenclature, classification systems, and concepts such as homology, isomerism, etc., are mere symbols by which compounds can be identified, classified and compared. But the formula is not the compound. The patentability of a compound does not depend on the similarity of its formula to that of another compound, but to the similarity of the former compound to the
latter. The thing that is patented is not the formula but the compound identified by it."

In the 1960s, lawyers thought that in order to prove the unobviousness of a chemical compound it was necessary to show that it had unobvious properties in comparison to known structural analogues or that the method of making it was not evident. Since these concepts of unobviousness have not been cancelled and other methods for determining unobviousness have not been published, these early principles can be used when looking at Markush structures. The main objectives of using them will be to make the writers of "super-nasties":

- define their core claims;
- show how the activity of the new compounds compares with that of known compounds; and
- narrow their claims.

Our confidence is based on the following considerations. They should highlight the weaknesses that very large, broad and unclear claims possess. The weak points are:

1. the multiplicity and variety of the structural fragments built into these broad generic formulae;
2. the absence of any clearly distinguished essential structural elements which determine the activity of the claimed compounds; and
3. the insufficiency or absence of experimental evidence of the utility of all types of compounds covered by the claims.

Points (1) and (2) make it much easier to select known analogues with the same activity from the prior art which can be used to challenge the application on the grounds of "obviousness". Additionally, (2) or (3) can facilitate opposition in those cases where there are few examples of analogues on the grounds of absence of proof of equivalence and, consequently, lack of unity of invention.

The broader and more convoluted the Markush structure, the greater the possibilities for the examiner to refuse the application on the grounds of obviousness due to the prior art. Importantly, this does not require a full novelty search, just the list of analogues that every examiner has to hand. The applicant will be forced to corroborate his claims with further specific examples and other supporting evidence. A carefully drafted patent with well established claims will have a blocking action proportional to its technical disclosures and to its lack of obviousness.

Conclusions

When patents on chemical compounds are granted with the view to giving the applicant the maximum monopoly, the rights of third parties are limited and the law becomes open to dispute.

The patent system must protect both the rights of the applicant and of the general public. For this, it is necessary that there are rules based on the fundamental concepts of both chemistry and patent law. The symposium appeared not to appreciate the first and to be confused about the second.

Whilst there is such disagreement between specialists, it is impossible to regulate patenting in the chemical area. This poses a serious problem as far as the patent law is concerned and causes distress amongst chemists as real chemistry gives way to "paper" chemistry.

References