Information about Microorganisms Contained in Patent Specifications

DIANE BANNISTER and CHARLES OPPENHEIM*

Centre for Information Science, The City University, London EC1, United Kingdom

Received December 7, 1978

Although patents are an important source for information on microorganisms, a survey disclosed that catalogs from culture collection depositories are unreliable in relating the availability with the microorganisms disclosed in a patent.

BACKGROUND

As a general principle of patent laws throughout the world, anything that occurs in nature cannot be patented. However, microbiological processes and products from such processes can be patented, and these have a long history.

A particular requirement of patent law is that the description in the patent specification should be sufficient to allow a skilled expert to repeat the experimental procedure. It is no easy matter to describe a microorganism in such a way that such an expert could obtain and use it, especially for *Actinomycete*, which even experts in taxonomy have problems with. In any case, a taxonomic description alone is not regarded as sufficient in U.K. or in U.S. patent law. These difficulties have led to a requirement to deposit the microorganism in a culture collection, and increasingly this requirement is becoming part of statute law. Thus, for example, in the U.K. an applicant for a patent is required to deposit any microorganism named in his application in a culture collection prior to the date of filing of the application. The name of the culture collection, date of deposit, and deposit number are also required. Other bodies also insisting on deposit include the Japanese, Canadian, Dutch, West German, Hungarian, and French patent offices and the European Patent Office (EPO).

Deposition in a U.S. culture collection is probably best if an applicant is likely to want protection in the U.S.A. at some time, because U.S. court decisions have held that deposit in a non-U.S. culture collection cannot be proven. The Budapest Treaty[1] would reduce this problem, because a deposit in a single culture collection acceptable to all members who have ratified it would be valid for patent applications in those countries. At present, only one or two countries have ratified this Treaty, but many are expected to do so over the next few years. Such cultures would be available to the public as soon as the patent or patent application becomes public knowledge. The Treaty requires that the collection maintains the strain for at least 30 years.

Many organizations, especially those in the pharmaceutical industry, have a considerable interest in the information available in patents on microorganisms and in obtaining samples of strains from culture collections. We decided, therefore, to carry out a study on the information on microorganisms given in patents and on the availability of microorganisms from the major collections.

QUESTIONNAIRES

A letter was sent to the information departments of 31 pharmaceutical firms known to be interested in antibiotics and with U.K. offices. This letter asked if these departments encountered any problems in obtaining information about microorganisms contained in patents. A questionnaire was sent to the internal culture collections of the same firms to determine their normal procedures for maintaining organisms and to find out if they had any problems in obtaining samples of strains from culture collections.

Another questionnaire was sent to the five U.K. and two U.S. culture collections required as depositories[2] by the EPO. Two other national U.K. culture collections not named by the EPO were also approached, but did not reply. A total of 71% of the firms replied in both cases, although 12 of the companies had no culture collections and 16 of the information departments did not handle that type of information. The response rate from the culture collections named by the EPO was 100%.

The information departments had never encountered any problems in obtaining information about microorganisms. Eight of the firms with internal culture collections provided interesting responses. All continue to maintain their own stocks of microorganism after deposition in a national collection. Parent strains were maintained even when the production strain was a mutant. Six of the firms were prepared to supply samples of strains to third parties from their own stocks under some or any circumstances.

Four organizations had experienced problems in obtaining strains from national collections and four more in obtaining strains from commercial organizations. Some had problems even after the grant of the relevant patent.

Turning to the national culture collections, one of the collections (NCDO, National Collection of Dairy Organisms) declined to answer on the grounds that it does not hold organisms named in patents. In fact, NCDO strain 1995 is mentioned in BP 1 433 328! This demonstrates that a collection may not necessarily be aware of patents naming them. All the collections that did reply maintain collections and these could, in theory, be used to find out about their holdings. In general, when the collection publishes a catalog, it will not list a strain deposited in connection with a patent application until the patent is granted or sometimes only after an official release has been obtained from the patentee. The collections differ on whether they require the permission of the depositor for release of a microorganism to a requestor after grant of the patent. Catalogs are usually cheap (they range from no charge to $10), but one of the collections (NRRL, Northern Regional Research Laboratory) does not publish a catalog and the others tend to be 3–7 years out of date. It is not unusual for 8 years to elapse between editions. The ATCC (American Type Culture Collection) is the best catalog from this point of view; it issues a new edition every two years. All this means that it can be difficult to check the availability of strains mentioned in recent patents.

In order to study this problem in more detail, we decided to take a sample of British microbiological patents and see if microorganisms mentioned in them appeared in the catalogs.

SELECTION OF A GROUP OF PATENTS FOR STUDY

We carried out a subject-matter search for all British patents published in the years 1948, 1958, 1968, 1970, 1972, 1974, 1976, and the first six months of 1978 for the following topics:

Antitoxins, toxins, toxoids, vaccines, etc.
Enzymes, proteins, and nucleic acids

0095-2338/79/1619-0123$01.00/0

Table I. Number of U.K. Microbiological Patents per Year

year	patents in sample	all U.K. patents	%
1948	19	15 558	0.12
1958	29	18 531	0.16
1968	86	43 038	0.20
1970	105	40 004	0.26
1972	133	41 609	0.32
1974	106	35 883	0.29
1976	99	41 755	0.24
1978 (1st 1/2)	31	19 529	0.16

Table II. Granted Patents (%) Filed Originally in Foreign Countries

	U.K.		U.S.A.		Japan	
	M[a]	all	M[a]	all	M[a]	all
1970	30	26	23	32	29	6
1972	29	24	22	31	27	8
1974	30	25	19	31	33	9
1976	35	21	13	26	32	10

[a] M = microbiology.

Beverages
Cultivating bacteria for use in microbiology
Antibiotics
Saccharides

In all some 1890 patents were studied. An unknown number of microbiological patents would be missed using these search headings. Of these, 608 were found to name microorganisms. Patents mentioning viruses, cell lines, protozoa, and higher life forms were not studied, nor were patents which concerned minor improvements to a known fermentation process unless they named specific microorganisms in the claims. The breakdown of patents by year is shown in Table I. These figures demonstrate that after increasing steadily in importance over the period 1948–1972, microbiological patents are now apparently declining in importance. This is also true for pharmaceutically related microbiological patents, which rose from 10 to 53 in the period 1948–1972, but then fell to 39 in 1974, to 26 in 1976, and to 8 in the first six months of 1978. This decline has been noted elsewhere.[3] These figures may, however, be unreliable because our search did not cover every microbiological patent published.

The 608 patents came from 32 countries, but the majority came from patents originally applied for in the U.K., U.S.A., and Japan. Table II demonstrates the importance of Japan in this respect. The percentage of patents in those which originate from Japan is about three times those for all U.K. patents emanating from Japan. The dominance of Japan was particularly marked in the fields of antibiotics, proteins, general microbiology, and saccharides.

Of the patentees, 218 were companies and the remainder were individuals, universities, etc. Only 27 firms had five or more patents in the samples and only one firm held more than 5% of the patents. Thus, this field is characterized by a diversity of competing firms from many countries.

In all, 190 genera and 829 species were cited by the patents. The numbers of named strains where a culture collection accession number was quoted is given in Table III. In all, 31 culture collections from 14 countries were named; 59% of the sample patents gave a deposit number for at least one strain, while only 35% gave a full description of the microorganism. About half the deposits were made in the country of filing the application. The most used culture collection was the ATCC (American Type Culture Collection), and not the NRRL (Northern Regional Research Laboratory), which does not publish a catalog. Patentees are clearly not concerned with limiting access to their strains by using the NRRL. Mention must also be made of the high use of Japanese culture collections. Obtaining samples would involve U.K. or U.S. users in long delays. U.K. culture collections are not used much.

Table III. Strains in Patents Citing a Culture Collection

	no. of strains cited
British culture collections (of which CMI[a] (27) and NCIB[b] (23) were the most cited)	61
U.S. culture collections (of which ATCC (503) and NRRL (141) only were cited)	644
Japanese culture collections (of which FERM[c] (69) and IFO[d] (68) were the most cited)	152
other culture collections (of which CBS[e] (34) was the most cited)	64
total number of strains cited	911

[a] Commonwealth Mycological Institute. [b] National Collection of Industrial Bacteria. [c] Institute of Microbial Industry and Technology. [d] Institute for Fermentation. [e] Centralbureau voor Schimmelcultures.

Table IV. Reliability of Culture Collection Catalogs

	no. of strains	no. correctly listed	strains not listed	no. incorrectly listed
four U.K. catalogs	129	37	83	9
ATCC catalog	584	479	47	58
total	713	553	130	67

HOW RELIABLE ARE CULTURE COLLECTION CATALOGS?

In order to examine this question, we obtained four of the U.K. culture collections' catalogs and an ATCC catalog. In each case, the latest edition was used. We then checked off each mention of a culture collection in a patent with the respective catalogs. Unfortunately, some patent specifications list strains without specifying species, and in other cases strains appeared in a patent specification under more than one heading. Inevitably, therefore, some strains mentioned in a patent will not be listed in a catalog. Nonetheless, as Table IV demonstrates, there is a clear discrepancy between information provided by a patent and information put into a culture collection catalog.

The ATCC catalog is clearly better at providing reliable information than the British catalogs, and this may be partly due to it being more up to date. The proportion of strains appearing under a different designation is due to the updating of the taxonomy of microorganisms. This represents a complication when searching for information on the strains. We found these "incorrectly listed" strains by using numerical lists of strains provided in most of the catalogs. However, the Commonwealth Mycological Institute and NCYC (National Collection of Yeast Cultures) do not provide such numeric lists, so inevitably incorrectly designated strains would not always be found.

We noted that over 80% of the deposits of microorganisms named in U.K. patents granted in 1978 were already to be found in the 1978 ATCC catalog. However, under the old British patent law, patents were granted relatively slowly, so this may be due to the earlier grant of a patent in another country.

CONCLUSIONS AND DISCUSSION

The now official need to deposit microorganisms named in patents into culture collections has been an unofficial need for

decades. Perhaps due to U.S. case law, the U.S. collections are the major depositories for microorganisms named in U.K. patents.

The questionnaire also revealed that difficulties have been encountered in obtaining the strains named in patents. The sample of British patents studied showed that some strains are not listed in current culture collection catalogs, or are incorrectly listed. It is theoretically easy to check that restrictions on the dispatch of strains to requestors has been lifted, as most culture collections do not list strains until after the grant of the patent. However, there is a complication in that many "current" catalogs are several years out of date, and of the ones studied only the ATCC has a practiced policy of publishing a new catalog every two years. Hence there is often a delay after grant of the patent before the casual enquirer can discover the status of a strain without writing directly to the culture collection. In addition, the NRRL does not publish a catalog, and all information on strains has to be obtained through communication with the collection.

The picture is further complicated by the fact that an appreciable number of strains have a different name in the patent and in the catalog. This is doubtless partly due to the uncertain state of some areas of microbial taxonomy, and to the not infrequent changes in microbial nomenclature. It is also likely that the employees of commercial organizations will not be experts in all areas of microbial taxonomy. Where culture collections have a numerical list of strains, an accession number has been given in the patent, and the catalog gives some details, such as depositor and patent number; this merely represents a time-consuming nuisance. But not all patents give an accession number, despite the fact[5] that U.K. law requires this. And not all catalogs have numerical lists of strains: the CMI and NCYC catalogs do not have such lists. Further, not all catalogs give enough details to allow the strain to be identified with certainty.

None of the catalogs studied here carry a taxonomic tree of the microorganisms, or details of genera which have undergone changes in name. So there are no clues to help the searcher find strains which are incorrectly listed.

It is therefore not surprising that U.K. law requires that the organism should be described in the patent, as well as deposited in a culture collection. The problems of taxonomy of actinomycetes, especially *Streptomyces* species, coupled with this requirement, results in some excellent descriptions of strains in some antibiotic patents, particularly where the strain is a new isolate. Such patents become a useful source of information on the strain concerned, and it would be interesting to know how many of these strains are later described in the journal literature, and whether any such articles carry as detailed a description as the patent.

In terms of the microorganisms, the sample patents were most useful as sources of information on actinomycetes, and least useful for algae, well-known yeasts, and disease-causing organisms. Information on other bacteria, fungi, and yeasts was intermediate.

The culture collection catalogs can form a useful quick reference source on microorganisms. The current NCIB and ATCC catalogs give considerable details of depositor, patents, and references to the strain in the journal literature, although the NCIB is discontinuing its policy of scanning the journals for references to NCIB strains.[6] Other catalogs, such as the NCTC and NCYC catalogs, give very few details, and are therefore only useful as a first check on whether the strain is available from the collection.

We therefore conclude that patents are an important source of information on microorganisms, a result that is in accord with other work emanating from this Department.[7] However, the unreliability of culture collection catalogs means that a searcher wanting to investigate a particular culture further may have problems finding out if a given microorganism can be obtained or if it has been mentioned in a patent.

REFERENCES AND NOTES

(1) "Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure", *Ind. Property*, 1–19 (1977).
(2) Anon., *Off. J. Eur. Patent Off.*, **1**, 34 (1978).
(3) C. Oppenheim, "The Importance of Industrial Property to the Pharmaceutical Industry", paper presented to 5th AIOPI Conference, 1978.
(4) C. Oppenheim, "Recent Changes in Patent Law and Their Implications for Information Services and Information Scientists", *J. Doc.*, **34**, 217–229 (1978).
(5) "The Patent Rules", Statutory Instrument 1978, No. 216, H.M.S.O., London, 1978.
(6) I. J. Bousfield, private communication.
(7) C. Oppenheim and E. A. Sutherland, "Case Study on Calvalume", *J. Chem. Inf. Comput. Sci.*, **18**, 126–9 (1978).

Substructure Search with Queries of Varying Specificity

ALFRED FELDMAN*
Division of Biometrics, Walter Reed Army Institute of Research, Washington, D.C. 20012

LOUIS HODES
National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20014

Received February 7, 1979

Efficient screening of queries of varying specificity requires a rich endowment of low specificity screens. However, most systems are heavily unbalanced toward high specificity. A more equitable mix can be achieved through use of the authors' method of screen generation.

INTRODUCTION

Systems using substructure search (SSS) depend on screens[1] to reduce the number of atom-by-atom searches. A measure of the power of a screening system is the closeness with which this number of atom-by-atom searches approximates the number of actual matches. In large files relatively few matches, proportionately, are usually required. Therefore, high screenout becomes almost synonomous with power in large files.

Generally, one wants the most powerful screening system for the widest collection of queries. Most screening systems work well on certain classes of queries but fall embarrassingly short on certain other classes. These often can be answered precisely only by virtue of an inordinate number of atom-by-atom searches for a few matches.

* Address correspondence to author at National Cancer Institute, National Institutes of Health, Bethesda, Md. 20014.