To keep INN or out
Sachin Bindal and Amit Koli

Ever since India opened up its patent regime in January 2005 to include product patents in the field of pharmaceuticals, the patent law in this domain has kept alive the interest of various stakeholders. This is rightly so, since India is also known as the pharmacy of the world and is a global market leader in the export of generic drugs to the United States and Japan, as well as to countries in Africa and Europe. The Indian pharmaceutical industry had a turnover of US$11 billion in 2010, registering a growth rate of 22 per cent. During 2013–2014, pharmaceutical exports stood at Rs 90 000 crores (US$14.55 billion). Also, India is one of the largest consumers of medicines in the world, even though accessibility of medicines across economically weaker sections remains an issue. The Indian patent regime is well equipped to balance the quid-pro-quo requirement of patents. Even though jurisprudence in this field is still evolving, recent judicial precedents have reaffirmed that this is so.

In 2013, the Indian Patent Office (IPO) proposed a requirement of disclosure of International Nonproprietary Names (INNs) in patent applications relating to pharmaceutical inventions. Thereafter, the IPO organized a meeting with different stakeholders to discuss the proposal and receive feedback on the feasibility and implementation of this policy. The proposal was to make the disclosure of INNs mandatory and for the Patent Rules to be amended to provide the necessary basis for this. The stakeholders put voiced their concerns both for and against the proposal. The IPO finally decided to reject the proposal at least of making this a mandatory requirement, so the Patent Rules remain unchanged. It goes to IPO’s credit that the proposal of mandatory disclosure of INNs in the patent specification was removed from the recently issued guidelines for examination of pharmaceutical applications. However, the guidelines instruct the examiner to search prior art based on any INN disclosed in the specification. Further, in the case of second medical use inventions, the examiner is directed to ask the applicant to disclose the INN of the known substance where second medical use is claimed. In the event that the applicant does not give such information even upon request, the examiner is required to seek to ascertain the INN and to search prior art based on it.

In this article, we attempt to explore the use of INNs as a proposed tool for searching prior art and examine whether INNs would indeed make things simpler for patent examiners in India.

The INN or generic name is an official name given to a pharmaceutical substance, as designated by the World Health Organization (WHO). An INN identifies a pharmaceutical substance or active pharmaceutical ingredient by a unique name that is globally recognized and

The authors

- Sachin Bindal and Amit Koli are Patent Associates with K & S Partners in Gurgaon, India.

This article

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easy to remember, unlike International Union of Pure and Applied Chemistry (IUPAC) nomenclature.

Apart from INN nomenclature, there are also various systems of nomenclature across different countries, such as British Approved Names (BANs) and United States Adopted Names (USANs) to identify pharmaceutical substance with an official nonproprietary name.5

Table 1 provides examples of INNs.

Table 1. Understanding INN

<table>
<thead>
<tr>
<th>IUPAC name</th>
<th>INN</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>N-(4-hydroxyphenyl)ethanamide</td>
<td>Paracetamol</td>
<td>Anti-pyretic</td>
</tr>
<tr>
<td>2-acetoxybenzoic acid</td>
<td>Aspirin</td>
<td>Analgesic, antipyretic, anti-inflammatory</td>
</tr>
</tbody>
</table>

The questions

The proposal for using INN as a search tool raised a number of questions, including the following: What makes INNs suddenly a sought-after tool for searching prior art patents? Would it be beneficial for the patent examiner to have a disclosure regarding INNs? Might it not be an extra burden on applicants seeking patents in India? Is there any vested interest of any group or agency in fueling the sudden need for such disclosure in Indian applications? Would this requirement be TRIPs-compliant?

INNs as a tool for searching earlier patents

The proposal to disclose INNs was based on the premise that this would help the examiner to conduct a search of prior patents more effectively.

To examine this hypothesis, we designed a sample prior patent search5 related to the method of synthesis for aspirin. The results are shown in Table 2.

We found that search string B, which used the IUPAC name of aspirin, found two relevant results out of four documents in the domain of method of synthesis of aspirin. In fact, string A appeared to have missed two most relevant results which were found by string B (as there are no common patents between string A and B as shown above). Thus INNs did not prove to provide an effective search tool in this instance.

Further, to confirm this provisional conclusion, we designed another study for prior patent search6 in the domain of composition of rotigotine. Rotigotine is a drug that was approved in Europe for the treatment of Parkinson's disease and restless legs syndrome in 2006. For this trial, we changed the subject matter of the search (from 'method of synthesis' to 'composition'), the name of drug molecule (from 'aspirin' to 'rotigotine') and the search field (from 'title' to 'title, abstract or claims' to broaden the patent search), as there may be a presumption that aspirin is a too old a drug, and String A would nevertheless miss patents in the domain of method of synthesis (where generally the IUPAC name is disclosed in synthesis patents). However, we reached the same conclusion as mentioned above. The results are shown in Table 3.

Out of four documents captured by String F, three documents belong to same patent family which discloses composition comprising acid addition salts of rotigotine, while one remaining document talks about novel rotigotine salts. In other words, these patents or applications were not relevant to our search, as they related to the domain of composition of rotigotine. Rotigotine is a drug that was approved in Europe for the treatment of Parkinson's disease and restless legs syndrome in 2006.

Table 2. Patent search related to Method of synthesis of Aspirin

<table>
<thead>
<tr>
<th>Search string</th>
<th>Type of search</th>
<th>Search string</th>
<th>Search field</th>
<th>Search jurisdiction</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. INN</td>
<td>Aspirin</td>
<td>Title</td>
<td>US, EP, EPb</td>
<td>417</td>
<td></td>
</tr>
<tr>
<td>B. IUPAC</td>
<td>Acetoxybenzoic</td>
<td>Title</td>
<td>US, EP, EP, WO</td>
<td>04</td>
<td></td>
</tr>
<tr>
<td>C. – D AND E</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>00</td>
<td></td>
</tr>
</tbody>
</table>


6 The patent search was conducted using the Total Patent database on 23 December 2014. ‘w/n’ is a search operator used in Total Patent database that finds search terms that appear within n-number of words of each other.
In addition, we designed one more study in the domain of the polymorph (crystalline) form of axitinib and found the same conclusion as mentioned above. The results are shown in Table 4.

Table 4. Patent search related to Polymorphs of Axitinib

<table>
<thead>
<tr>
<th>Search string</th>
<th>Type of Search</th>
<th>Search String</th>
<th>Search Field</th>
<th>Search Jurisdiction</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>G. INN</td>
<td>Axitinib</td>
<td>Title or, Abstract or, claims</td>
<td>US, EP, WO</td>
<td>331</td>
<td></td>
</tr>
<tr>
<td>H. IUPAC</td>
<td>Pyridin w/10 indazol w/10 sulfanyl</td>
<td>Title or, Abstract or, claims</td>
<td>US, EP, WO</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>L. –</td>
<td>D AND E</td>
<td>–</td>
<td>–</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

Date of Search: 14 April 2015 on the Total Patent Database.

Why link patents to INNs?

Was it a good idea to link patents to INN? If it was, who should take on the burden of linking patents to INNs? Would the applicant have found it unnecessarily cumbersome to disclose the INN before filing the patent application? At best, any link between the patent and the INN should be the responsibility of regulatory bodies during the drug approval stage.

Including INNs at the time of filing the patent application

Drug patents are filed as soon as the pharmaceutical research and development (R&D) shows promise in an invention. Accordingly, compounds of interest are unlikely to have an INN at the patenting stage. Some patents actually use laboratory acronyms for naming these compounds. It is therefore a practical challenge to include the INN at the time of filing of a patent application, which is why patent applications almost never use INNs. Besides, since the international patent system does not allow for adding subject matter once the application has been filed, the inclusion of an INN does not present a viable approach.

Internationally, linking patents to INNs is done at the regulatory stage when applying for drug approval and not at the patenting stage itself. Patent linkage at the product approval stage is meant to prevent patent infringement by generics and is followed by several countries that are members of the World Trade Organization. Further, such linkage requires a closer collaboration of health regulators and the patent office.

The US Food and Drug Administration (FDA) used to link approved drug products (which had an INN) to patents on their website using a repository known as the Orange Book.

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Orange Book. We performed the search for ‘rotigotine’ (an FDA-approved drug acting as dopamine agonist indicated for the treatment of Parkinson’s disease and Willis-Ekbom disease) as an INN in the Orange Book. The search results are presented below in Table 5.

Table 5. Orange book patents of Rotigotine

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Rotigotine</td>
<td>6699498</td>
<td>27 November 2020</td>
</tr>
<tr>
<td></td>
<td>6884434</td>
<td>30 March 2021</td>
</tr>
<tr>
<td></td>
<td>7413747</td>
<td>18 March 2019</td>
</tr>
<tr>
<td></td>
<td>8246979</td>
<td>1 September 2027</td>
</tr>
<tr>
<td></td>
<td>8246979</td>
<td>1 September 2027</td>
</tr>
<tr>
<td></td>
<td>8246980</td>
<td>27 November 2025</td>
</tr>
<tr>
<td></td>
<td>8617591</td>
<td>22 July 2023</td>
</tr>
</tbody>
</table>

Patent information corresponding to a drug product is submitted by the sponsor/applicant to the FDA, depending on the approval status of the product application. Following the product’s approval, the FDA publishes the list of patents mapped with that product (which has an INN) in the Orange Book.

A few years back, a decree was published in the official Gazette of the Federal Government of Mexico, which amended the Regulations of the Health Law as well as the Regulations of the Law on Industrial Property. This new amendment imposed upon the Mexican Institute of Industrial Property (IMPI) an obligation to publish a special gazette listing those patents relating to allopathic drugs and their corresponding INNs. This new regime was brought in to benefit patent owners, as following this amendment, the Mexican health authorities would not grant health registrations for products covering the active ingredients as published in the gazette, until the expiry of the patent.

In this case, applicants for marketing approval of pharmaceutical products are required to inform the health regulatory authorities whether or not they are the patent holder or licensee for any existing patent relevant to that product. An the applicant who does not have a patent or licence must provide a declaration that the product application does not infringe the rights of the patent holder.

The health authorities work with the IMPI to determine the patent status of the product for which there is a pending marketing application. If the search indicates that a valid patent would be infringed, the health authorities will give the applicant an opportunity to demonstrate that it has the rights to the product. In the alternative, the health authorities will reject the product application.

Similarly, in China, the State Food and Drug Administration (SFDA) maintains two separate tracks by which it provides patent linkage for compound/composition patents:

- The SFDA requires all applicants for marketing approval to check patent status prior to making an application, and to certify that their products do not infringe any existing patents; they must also acknowledge liability for damage resulting from any future finding of patent infringement.
- The SFDA maintains a list of all drug product registrations by chemical names (INNs), which is available for frequent inspection by patent owners, who can check whether there are applications for marketing approval for new products that may infringe any existing patents.

In the interest of the patent owners and in order to avoid copying of a patented drug, such linkage between patent and INNs at the regulatory stage does appear justified. The aim of the INN system has been to provide health professionals with a unique, universally available, designated name to identify each pharmaceutical substance. The existence of an international nomenclature for pharmaceutical substances, in the form of INNs, is for identification, safe prescription and dispensing of medicines to patients, and also for communication and exchange of information among health professionals. The role of INNs is mainly for regulatory and commercial purposes and not for patenting issues. Readers may also recall that, in Bayer v Cipla, the Indian High Court and the Indian Supreme Court clearly ruled that there can be no overlap between regulatory and patent law. This would also apply in the present context where the regulatory and commercial role of INNs should not
overlap with the patent by disclosing an INN in a patent application.

**What would it take to disclose an INN in a patent application?**

INNs are allocated by the WHO on the advice of experts from the WHO Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations. The process of INN selection follows three main steps:

1. a request/application is made by the applicant company;
2. after a review of the request, a proposed INN is selected and published for comments;
3. after a time-period for comments and objections has lapsed, the name will obtain the status of a recommended INN and will be published.

Importantly, the rules relating to the application for an INN specifically state that an INN for a substance should only be applied for once it has been tested on human subjects.

**Concerns of the patent applicant**

Patent applicants seeking a drug patent in India have had substantial concerns with regard to the inclusion of INNs in the patents’ description. These concerns include the risk of losing novelty due to delay in obtaining an INN from the WHO; the lack of clarity as to the consequences of not including an INN in the description (even though the recent examination guidelines on pharmaceutical inventions issued by the IPO do not mandate the disclosure of INN now); possible loss of patent term, where the IPO decides to withhold the grant of a patent for want of INN disclosure; misuse by third parties due to frivolous oppositions or invalidation proceedings, particularly on the ground of s 3(d) of Indian Patents Act; and practical difficulties in specifying INNs for all possible components of a claimed composition or a Markush representation.14

Section 10(4) of the Indian Patents Act clearly defines what the specification of the patent application shall contain. The ‘best method of performing the invention’ requirement under s 10(4) (b) of the same Act clearly states that the applicant/inventor is entitled to protection by disclosing the best method of performing the invention. The disclosure of an INN does not appear to be a reliable source of describing an invention; nor does it provide any aid in enabling a person skilled in the art to carry out or apply the invention. It is only wise that this requirement should be dropped: it imposes a burden on the applicant, who in any event must overcome other important legal barriers before obtaining a drug patent in India.

Legally speaking, under Article 27 of the Agreement on Trade-related Aspects of Intellectual Property Rights (TRIPS), members of the said agreement cannot discriminate between different fields of technology in their patent regimes. By rejecting the proposal for mandatory requirement of disclosing an INN in the specification, India has saved itself from being potentially accused of discrimin-

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14 Herein, Markush representation are chemical symbols used to indicate a collection of chemicals with similar structures. They are commonly used in chemistry texts, and also in patent claims.
ation between other technologies and pharmaceuticals, which would be contrary to TRIPS.

From sudden interest to careful thought
The sudden interest of the Indian Patent Office in require disclosure of INN in a patent application came as a surprise to patent applicants in the pharma domain. Given that debate over the patenting of pharmaceutical inventions in India is no longer restricted to legal issues but evokes serious emotive issues, the IPO was certainly faced with dilemma of having to address both. Admirably, the IPO took a reasonable and balanced view on this issue pursuant to elaborate discussions on this issue with various stakeholders. It may augur well for the patent fraternity if the IPO thoroughly researches the need and usefulness of such proposals, which have a great impact on all the stakeholders before initiating any nationwide debate.

The patent search outlined in Table 6 was performed in Total Patent Database on 15 April 2015. The Search field remains the same as Title, Abstract or claims in US, EP and WO. The same conclusion was drawn as mentioned above, i.e. that the strings based on INN missed the relevant results which were captured by the strings based on the IUPAC name.