Comments of the Biotechnology Industry Organization (BIO)

To the Office of the Controller General
Patents, Designs and Trade Marks,
Government of India

Regarding the Draft Guidelines for Examination of Biotechnology Applications

18 January 2013

The Biotechnology Industry Organization (BIO) appreciates the opportunity to provide comments in response to the Controller General of Patents Designs and Trademarks in India on the "Draft Guidelines for Examination of Biotechnology Applications" hereafter referred to as "Draft Guidelines", or "Guidelines".

About BIO and the Biotechnology Industry

The Biotechnology Industry Organization (BIO) is a non-profit organization with a membership of more than 1,100 biotechnology companies, academic institutions, state biotechnology centers, and related organizations worldwide. BIO's members are involved in the research and development of healthcare, agricultural, industrial, and environmental biotechnology products. In India, BIO's members have partnered with Indian companies, built research facilities and are collaborating with its research institutions. India itself, boasts over 350 biotechnology companies employing over 20,000 scientists and contributing over US$ 2 billion to the Indian economy.

Currently, the biotechnology industry is a thriving, competitive, and dynamic industry for many countries, including the U.S. and many European countries. A significant reason for this growth is the availability of comprehensive and effective patent protection for biotechnology inventions. These inventions include isolated nucleic acid and proteins, micro-organisms and cell lines-- all of which are afforded patent protection by both the U.S. and Europe. Moreover, in the case of the U.S. and Europe, modified plants and animals are also patentable. Such innovations enable start-up companies, universities and established companies to justify the significant investments – whether on the order of millions or hundreds of millions of dollars – that are necessary to discover, develop, bring to market and support products and services based on these nucleic acid inventions.

India has recognized the benefits of biotechnology, not only to address health and energy concerns, but also to unleash India's significant economic potential. Indeed, India has invested billions of dollars into biotechnology and has developed a national biotechnology strategy that calls for among other things predictability in the IP system. The country is on the cusp of realizing much of its investment in the biotechnology sector. As such it is critical that the policies of one agency within the government not undermine the significant investments made by another agency within the government.

The Biotechnology Industry

The life sciences industry in India, as anywhere in the world is fueled by the strength and predictability of the patent system. This is because biotechnology research and development is both risky and resource and time intensive. On average, it takes more than 10 years to develop a biotech medicine or a plant improved through agricultural biotechnology from its inception to regulatory approval and finally to market launch. The average, fully capitalized cost of developing a new medicine has been estimated at USD$1.2 billion and a new biotechnology derived plant product at USD$133 million. Most biotechnology innovation begins in the laboratory where a particular gene of interest is identified in association with some biological phenomenon. This gene may have some correlation with a specific disorder or disease or perhaps a new plant trait or enzyme. Further research and development of these promising discoveries can take years, even decades, and hundreds of millions of U.S. dollars to achieve. Biotechnology innovators generally patent these promising discoveries to a) increase the likelihood of further research, development and commercialization of these discoveries by the innovators or on their behalf, b) generate interest from investors to further research on these discoveries; and/or, c) license them to potential partners or developers. In these situations patents are used as instruments to assure investors that their investment is secure and has the potential to be recouped and is transferable. Thus it is no surprise that inadequate patent rights, or an absence of patent rights, will severely hinder the development and commercialization and hence the availability of promising biotechnology discoveries.

Biotechnology innovation requires predictable and effective IP protection throughout the research, development and commercialization process, including upstream (early stage) and downstream (product) IP protection. Such upstream protections generally include broad patent eligibility for biotech innovations, consistent patent term, flexible licensing practices, and effective patent enforcement. Downstream protection is just as important, for example in the drug industry, as a significant portion of the development time and money goes towards generating the regulatory data package that is required by various regulatory authorities. Therefore, downstream protection for biotech products must include sufficient protection against competitors relying on the innovator's data package to secure abbreviated approval of competitive products in such markets.

Given the importance of patent protection for biotechnology product development and commercialization, a streamlined process for patenting, and the appropriate scope and subject matter protections are of great importance.

Therefore, changes to the law or guidance which affect the patentability of biotechnology inventions are extremely important to our members. In particular, in India, where both the public and private sectors are potentially interested to invest heavily in biotechnology, or to conduct research which may result in numerous discoveries in biofuels, healthcare and in agriculture, a patent framework that facilitates the translation of these discoveries to products will be of great value.

Draft Guidelines

Given the importance of protections for basic biotechnology inventions to the survival of the biotechnology sector in India, BIO has reviewed the Guidelines and is pleased to provide suggestions for possible improvement within the framework of the Indian patent law. At the outset it is important to note that BIO recognizes there are countries, including India, that view aspects of biotechnology to be controversial. BIO supports, and often participates in robust discussions on ethical issues pertaining to biotechnology. Indeed BIO's Statement of Ethical Principles espouses the use of biotechnology in a socially responsible manner to save or improve lives, improve the quality and abundance of food, and clean up hazardous waste. http://www.bio.org/articles/bio-statement-ethical-principles

Nevertheless, BIO recognizes, as does India, that such soaring goals cannot be met without the appropriate legal and regulatory framework, and the necessary investment. Biotechnology is a global industry. As such biotechnology inventors file for patent protection in many different jurisdictions for the various reasons stated above. While patent protection is territorial, inventors, in general, expect to find relative consistency in most jurisdictions. For example, what is considered an invention in the U.K. is most likely patentable in the U.S. or in India. Accordingly, to the extent possible, patent office guidelines should provide uniformity in examination and direction to the examining corps, while at the same time being relatively consistent with other jurisdictions. In this regard, BIO's comments reflect the experiences of our members in varying jurisdictions.

As a general comment, the Draft Guidelines provide several Illustrative Examples attempting to show what subject-matter may not be allowable under the considered provisions. For a complete guidance of the examiners, it is suggested to include more illustrative examples showing what subject-matter could be allowable.

Paragraph 6.

BIO notes that the claims of biotechnological inventions recited in the Draft Guidelines include the various inventions listed above, including polypeptides, nucleic acid sequences, cells and microorganisms etc. BIO recommends that the guidelines reflect that the categories of claims referred to be understood to be those that are "isolated or engineered", e.g. "isolated or engineered polypeptides", "isolated or engineered polynucleotides" etc. Indeed, when a biotechnological invention is claimed in a patent application, it is always after the inventor has isolated it from nature. Nucleic acids, proteins and antibodies are not found in nature in isolated form. Similarly, nucleic acids, proteins and microorganisms that have been engineering to have different compositions (e.g., different sequence) than found in nature should also be considered patentable. Please see also comments on this point related to section 11 below.

Paragraph 8.2

The example pertaining to a library sequence in this section is unclear. The Guidelines can be improved by either deleting this example or providing further explanation. On its face, the example is inconsistent with the standards of most jurisdictions. According to many jurisdictions, the availability of a polynucleotide library (e.g., through sale or offer for sale) would not bar the patentability of a hitherto unknown polynucleotide sequence in the library. The particular polynucleotide invention would need to be defined in sufficient detail so that a patent application could be filed or that the invention could be carried out. The absence of the isolated nucleotide sequence at the time that the library was available would generally render the isolated nucleotide sequence patentable in most jurisdictions.

Paragraph 9.

The Guidelines reflect a stronger presumption of obviousness than what exists in most jurisdictions. In particular, the Guidelines seem to direct the examiner to engage in hindsight reconstruction. For example, the Draft Guidelines state that it would be sufficient to "show similarities" in the structure of a claimed structure and a prior art structure, as well as activity. The Guidelines rely on the case of Hoffmann-La Roche Ltd & Anr. Vs. Cipla Ltd-- a judgement of the Division bench during interim injunction arguments. However, it is important to point out that on Sep 7, 2012, the Delhi High Court after hearing evidence in this case, held that mere structural similarity does not render the invention obvious. Given that this decision was final after evidence presented, it supersedes the decision of the Division bench which was at the interim stage. Thus, BIO submits that the application of this decision in addition to the various supporting statements in the Guidelines pertaining to "similarity" are not accurate.

Moreover, given that the standard here is inventive step or obviousness, there must be a motivation in the prior art to change the structure of the prior art to the claimed structure. If, for example, the recognition of the existence of a problem in a particular structure was absent from the prior art, then such motivation to change structure to solve the problem could be the inventive step that would render the changed polypeptide structure patentable over the prior art. Moreover, there must be a reasonable expectation of obtaining a specific result. The Draft Guidelines disregard the possibility that the art may not provide a reasonable expectation of success. In most jurisdictions, the motivation to combine two products is not indicative that a person of ordinary skill in the art will have a reasonable expectation of achieving the desired result. This additional element has been developed by various patent offices over time for inventions in the fields of chemistry and biotechnology. In this field, inventors often it necessary to try many technical approaches or combinations, which could *prima facie* all have appeared obvious to try based on similarities in structure and activity, but from which only one approach would have appeared to really have an effect. This inherent property of the chemical and biotechnological arts gives inventors only a very limited level of expectation of success absent a compelling indication in the prior art, which is recognized by patent offices such as the EPO or the USPTO, and which the BIO members would appreciate to see recognized in the Indian Guidelines.

The assessment of inventive step is fact- dependent and should be assessed on a case by case basis. A one-size fits all approach set through general guidance has the potential to prevent patents on innovative biotechnology products, thereby stifling innovation in this sector. As mentioned previously, BIO members file patent applications in many jurisdictions most of which are members of the Patent Cooperation Treaty (PCT) , in the hopes of launching key products in those markets. Such divergent protections between key markets would create problems for biotechnology companies and may affect business decisions with respect to those products. In addition, such a strict approach to patentability is likely to discourage research and development activities in the area of biotechnology in countries that implement them .

The two illustrative examples given in relation to the mutated polynucleotide/ polypeptide (page 9) appear to draw a "level" that an effect would need to reach in order for the inventive step criterion to be fulfilled. However, since an assessment of inventive step is based on a new structure and an associated effect, a proper assessment of this criterion should not include a level that such an effect should reach, especially in quantitative levels. A primary reason is that

such improvements are specific to each invention, and examiners from whatever jurisdictions have no means to evaluate the value and importance of an allegedly small improvement. In the biotechnological field, like in the chemical field, even what may be perceived quantitatively as a small improvement in activity could have a critical value, and inventive step should be recognized for it. BIO proposes that the two Illustrative Examples in paragraph 9 be amended to reflect these considerations.

Paragraph 10. Section 3 (b)

The Draft Guidelines recite a non-limiting list of inventions that it considers to be contrary to morality or which cause serious prejudice to human, animal or plant life or health or environment. The biotechnology sector is making significant advances in the area of stem cell research-- albeit significant additional investment is required so that resulting products can provide benefit to society. It is not clear whether certain types of cells, such as embryonically derived stem cells that are therapeutically useful would also be considered as unpatentable subject matter. BIO recommends that the Guidelines be amended to allow for the patenting of stem cells and other modified cells that can be useful for therapeutic purposes.

The Draft Guidelines also indicate that "a process for preparing seeds or other genetic materials comprising elements which might cause adverse environmental impact, like terminator gene technology" should be regarded as excluded under section 3(b). However, it appears unlikely that patent examiners could be in a position to assess whether an invention "might cause adverse environmental impact". It is therefore submitted that patent applications on such inventions preferably never be rejected under this section solely based on examiners and patent office's assessment, but only when a separate national agency or authority assessing and deciding on safety matters has issued an official decision that any such technologies are effectively banned due to their likelihood to cause adverse environmental impact. Moreover, the example given of the terminator gene technology is not known to the BIO members as an element which might cause adverse environmental impact.

Paragraph 11. Section 3(c)

The Draft Guidelines state that products such as microorganisms, nucleic acid sequences, proteins, enzymes, compounds, etc. which are directly isolated from nature are not patentable subject matter. BIO has significant concerns with this statement as it denies patent claims for essentially all of the basic biotechnology inventions which are necessary to the further research and development of

innovative biotechnology products. This is contrary to the laws of many jurisdictions which for example allow for the patenting of isolated nucleic acids, micro-organisms, proteins etc as they do not occur in nature in isolated form. The Guidelines in an earlier section pertaining to industrial application admit that a test for patentability is whether the claimed invention has a specific, substantial and credible utility associated with it. As an illustrative example, an isolated nucleic acid with a discrete sequence that has been found to be linked with diabetes, for example, would have a specific, substantial, and credible utility, and therefore should be considered patentable under the Guideline's own earlier test. Moreover, patented isolated nucleic acid molecules are stripped of everything that is necessary for the normal operation of a gene in its natural state. This results in nucleic acid molecules that do not exist in nature. Such nucleic acid molecules can be used in ways that are simply not possible with the natural gene – for example, to conduct gene transfer experiments, to make DNA vaccines, or to produce therapeutic proteins in large scale cell culture.

Moreover, the law refers to discoveries, even "mere discoveries", which is understood as referring to acts of identifying that certain elements found in nature have a particular effect, but without bringing such elements in a useful form. It is well known in the field of biotechnology that elements of nature can only be useful when provided in an isolated form. Therefore, an isolated form is the result of an action of man on nature, beyond the mere identification (or discovery), to provide a product of nature in a useful form. It is therefore suggested that such an isolated form should not be interpreted in the Guidelines as relating to a mere discovery.

A similar argument applies to proteins and polypeptides. Proteins do not exist in nature in isolated form. They are generally associated with many other proteins and molecules making them unvendible. Many jurisdictions also allow the patentability of microorganisms. Indeed, even the Calcutta High Court concluded that a new and useful end product that contains a living organism is patentable. Biotechnology companies conduct research and development on microorganisms that can be employed in water cleanup, energy creation and other environmental applications. Thermophilic bacteria, for example, have been proven to be of great importance in the biotechnology sector for applications in biomass conversion and in the development of biofuels, and are the basis on which companies obtain funding to further their research.

On a further clarifying note, the illustrative example in this section refers to rDNA. The art recognizes two different definitions of rDNA- recombinant DNA or ribosomal DNA, which is DNA encoding ribosomes. It is not clear to which form of DNA this example refers.

Paragraph 12. Section 3 (d)

In this section, the Draft Guidelines direct examiners to reject claims under 3(d) if there is no improved property/efficacy of the modified substance established. The definition of efficacy according to the illustrative examples appears to be solely based on therapeutic efficacy. This requirement excludes from patentability many significant inventions in the pharmaceuticals area, e.g., new forms of known substances with improved heat stability for tropical climates, or having safety or other benefits that may not result in "enhanced efficacy" *per se,* but would result in a useful therapeutic window (range of drug dosages which can treat disease effectively while staying within the safety range) without which such drug would not be desirable. Even if not removed, new forms of a substance that has benefits to the patient with clear support for its therapeutic improvement should be central to the concept of "improved efficacy" yet are noticeably absent in consideration for granting a patent. Indeed, the improved efficacy concept should not be limited to "significant" enhanced efficacy. First, because this requirement is not in the law. And also because examiners are not in a position to determine what would or would not constitute a significant improvement. As long as an improved efficacy is demonstrated in the specification, it is submitted that patentability of the claimed new structure should not be excluded from patentability based on this section. Indeed, this section should be interpreted in line with the general patentability criteria of novelty, inventive step and industrial application. In addition, this provision appears to be inconsistent with India's obligations pursuant to Article 27 of the TRIPS Agreement, which requires that patents be made available to "any inventions … in all fields of technology, provided that they are new, involve an inventive step and are capable of industrial application." Section 3(d) also creates an additional hurdle to patentability that is applied only to certain chemical products, and therefore appears to violate the non-discrimination clause with respect to field of technology set forth in TRIPS Article 27.

Paragraph 16.Section 3(j)

Although no details and examples are given in the Draft Guidelines as to the exclusion of plants, BIO members are usually exposed to an exclusion of any claims reading on plants by the Indian patent examiners, and would therefore like to comment in that respect.

The PPV&FR Act, 2001 protects plant varieties, and plant varieties correspond to the lowest known botanical rank. However, certain biotechnological inventions, like e.g. a new gene, usually apply to more plant varieties than a single plant variety, and usually apply to at least a plant species, if not to most plants.

Thus interpreting Section 3(j) as excluding all claims on plants beyond the botanical level of the plant variety leaves inventors of biotechnological inventions that apply to more than a single variety of plant, without protection for their invention. If a new gene construct for use in plants is recognized as patentable by the Indian patent office, any claims to "plants" containing such gene construct become rejected based on a broad interpretation of Section 3(j), and the patent becomes useless to the inventor since the patentable genetic construct can then be used by anyone else in plants. And using the PPV&FR Act, 2001, for that purpose would not be possible as it would amount to filing an application for protection under this Act for each and every known plant varieties containing such gene. It is therefore proposed that the Controller General of Patents Designs and Trademarks in India takes this opportunity to amend the Guidelines to declare that the exclusion of plants under Section 3(j) should be interpreted narrowly (like exclusions should generally be interpreted in most jurisdictions), and that this exclusion should be interpreted as solely excluding plant varieties, and therefore as allowing a claim on a plant or a plant species containing a patentable invention.

Providing protection for such biotechnological inventions can incentivize R&D in this area, and can yield positive economic and societal impact. This phenomena is recognized by Agriculture Minister Sharad Pawar in a recent article in the Press Trust of India, New Delhi, where he stressed the importance of the importance of genetically modified foods in India for food security and continued scientific innovation and economic growth.

Paragraph 18. Section 3 (p)

The Draft Guidelines in Example 1 appear to provide that claims to a specific extract may be rejected in view of more general prior art that contains a plant with a purified extract. This example implies that patents on an invention that may use materials previously used in traditional medicine or other traditional fields would be prohibited regardless of whether it is novel, inventive or has industrial applicability. BIO urges that all applications should be treated on a case-by-case basis, as indicated under the Indian Patents Act, for novelty, inventive step, sufficiency of description, etc.

Paragraph 19.

The Guidelines in this section seek to address sufficiency of disclosure for the purpose of enabling a claimed invention. However, it is unclear from this section what the standard is for assessing sufficiency of disclosure and whether it has basis in case law. Moreover, BIO submits that if a patent application lacks

sufficiency of disclosure, once published, then it should not be viewed as prior art with respect to a later filed application when making determination of anticipation or inventive step.

Paragraph 21.

In this section, the Guidelines refer to biodiversity related issues. India's Patents Act and the Draft Guidance require applicants to disclose the source and geographical origin of biological materials used to make an invention that is the subject of a patent application. These special disclosure requirements impose unreasonable burdens on patent applicants, subjecting valuable patent rights to great uncertainty. While the Guidance requires that an objection be raised to conform with the requirements, under the Indian law, the failure to identify the geographical source of a biological material **and** its origin may be a basis for opposition or revocation proceedings. However, the necessary relationship to the patented invention is not clear and their impact is inherently retroactive in effect. For example, companies often have obtained samples or materials from universities or in partnership with universities or depositories. Identifying the source of these materials may be impossible as many may have been obtained decades prior to eventual use and filing of a patent application. These requirements pose unacceptable risks for patent applicants and undermine the incentives of the patent system to promote research and innovation in the biotechnology sector.

Moreover, such requirements do not further the objectives of the CBD, which we understand to be the intended objective. Instead, an effective ABS regulatory system, based on mutually agreed terms between the provider and user of genetic resources, which may include terms relating to future intellectual property rights based on use of such resources, is the best mechanism to ensure furtherance of the ABS objectives of the CBD. This approach should apply for all uses of genetic resources, whether those uses are subject to intellectual property rights or not.

BIO appreciates the opportunity to provide these comments for your consideration and is available to discuss these issues in greater detail at your convenience.

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