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Connecticut High-Tech Company Uses "Nature's Fingerprint" To Add Value to Patent Portfolios

By Anthony D. Sabatelli, Ph.D., J.D.*

It is not often a company puts forward truly breakthrough technology that is both elegantly simple and yet scientifically sound. A New London-area scientist has found a unique way to read the naturally-occurring molecular fingerprint of drug products and their synthetic pathways to help pharmaceutical companies enforce their hard-won patent rights against infringers.


Dr. John Jasper

Dr. John Jasper, chief scientific officer of Nature's Fingerprint®, a division of Molecular Isotope Technologies LLC (or MIT LLC for short), is the guy who has made practical use of this fingerprinting technology. "What we are doing is measuring chemical tracers, also known as isotopes, to determine the origins of drug products and pathways to help pharmaceutical companies and law enforcement authorities combat counterfeiting", says Dr. Jasper. "The distribution of natural isotopes in a drug product is analogous to the highly-specific pattern of a human fingerprint. It is this fingerprint of nature that can be used to almost unequivocally identify the source or process for a given drug product."

I was originally asked to interview Dr. Jasper, because it was thought a practicing biotech patent attorney, such as myself, would be uniquely suited to tell his story, a story that is at the intersection of science and patent law. I recently had lunch with him to learn firsthand about this unique fingerprinting technology and its applications, and in particular how it is being used to help the pharmaceutical industry strengthen and enforce its patent portfolios.

The History of Isotopes

Dr. Jasper recounted how large-scale scientific research involving both radioactive and non-radioactive (*i.e.* stable) isotopes goes back to the time of the Manhattan Project, which produced the first atomic bombs during World War II. Isotopes – whether stable or radioactive – are forms of the same chemical element having different atomic masses. For example, uranium has an isotopic form with a mass of 235 and also an isotopic form with a mass of 238. Dr. Jasper's firm, MIT LLC, focuses solely on non-radioactive, stable isotopes.

By 1942, isotopes had only been known for about thirty years. Most of the research involving isotopes had been theoretical, relating to determining atomic structures and studying the then-mysterious properties of radioactivity. The Manhattan Project changed all that. The dire urgency of the war effort led to the development of sophisticated techniques for separating and identifying isotopes. One of these techniques, Isotope Ratio

Mass Spectrometry (or IRMS for short), which is used to measure the relative abundance of isotopes in a sample, is now an important tool in the field of those studying and using isotopes.

Dr. Jasper explained that when he came on the scientific scene in the 1980s he already had an interest in isotopes. In 1988 he earned his Ph.D. thesis from the Massachusetts Institute of Technology/Woods Hole Oceanographic Institution Joint Program in Chemical Oceanography, where he assessed the isotopic composition of bulk organic matter and specific biomarker concentrations in deep-sea sediments to understand the effects of climatic changes. As a postdoctoral fellow at the Biogeochemical Laboratories at Indiana University in Bloomington he used isotopes to reconstruct dissolved carbon dioxide levels in ancient oceans. After leaving academia, Dr. Jasper worked at Pfizer Inc. in Groton as a research scientist where he began to develop his interests in the potential use of isotopes in pharmaceutical research.

Nature's Fingerprint is Born

In 1999 Dr. Jasper formed a company, MIT LLC, around the premise that stable isotopes could be used to specifically identify individual batches of pharmaceutical materials. He said "we had shown that every lot or batch of pharmaceutical products had their own highly-specific 'isotopic fingerprint'. We subsequently realized the potential applications of our technology to provide forensic support for patent infringement and enforcement efforts had just opened up immensely."

The technology developed by MIT LLC is sufficiently unique that it has been awarded two US patents, the most recent of which issued this past February. This latest patent relates to methods and systems to correlate a product such as a pharmaceutical to the synthetic process by which it was made. In other words, the method is a means of finding the "smoking gun" of the patent infringer. This patented technology used by Dr. Jasper and his company is known under the trademark "Nature's Fingerprint®". Even the FBI has recognized the value of this unique technology, calling upon Dr. Jasper for advice during the anthrax scare that occurred post 9/11.

Recently, Nature's Fingerprint® joined CURE (Connecticut United for Research Excellence), an entrepreneurial cluster of local biotech, pharmaceutical companies, academic institutions, service providers, and government agencies. Dr. Susan Froshauer, president of CURE, said "we are excited to have a company such as Nature's Fingerprint® join our ranks. Dr. Jasper brings world class technology to help the pharmaceutical industry with the not-so-easy task of monitoring and enforcing their intellectual property rights. By doing so he helps add tremendous value to their drug pipelines in which they have invested millions of dollars of research and many years of development time." CURE further recognizes the value of Dr. Jasper's company in protecting patent rights by aptly describing Nature's Fingerprint® on their website, www.curenet.org, as "an intellectual properties' firm".

Adding Value to Patent Portfolios

So how exactly does Nature's Fingerprint® add value to the pharmaceutical industry and its patents? Before answering this question it should be briefly explained what is at stake.

It is well recognized that pharmaceutical research is a high-risk and expensive undertaking. It takes many years and huge investments to bring a new drug product to the marketplace. This is not surprising considering that a single human Phase III clinical trial can easily top $50 million dollars to run. Phase III is the last stage of clinical testing before a pharmaceutical developer submits an application for drug approval to the US Food and Drug Administration (FDA). The FDA typically requires two such "well-controlled" studies for drug approval. According to the Tufts Center for the Study of Drug Development, which has been tracking the cost of prescription drug development for over thirty years, the cost of developing a single new drug was estimated at $1.2 billion in 2006. On top of this immense cost, the average time for bringing a new drug to market from its original inception in the lab is now over ten years. Finally, the success rate for prescription drug development is quite low − by some estimates, only about one in twenty drugs make it all the way from initial Phase 1 human clinical trials to the marketplace. Going back even further to inception at the lab bench, the success rate might be just one in several thousand.

The main way to secure protection for new pharmaceutical products is through sound patent protection. However, the cost of patent protection is high and time consuming. The "gold standard" in patent protection for a new, small organic molecule drug product is a composition of matter patent. Such patents specifically describe or "claim" the drug compound, and preferably a broader genus of chemical structures surrounding that compound. Furthermore, the cost for filing, obtaining, and maintaining a single patent across a broad range of countries can cost tens of thousands of dollars, and in many instances can easily top a half a million dollars.

However, it is not always possible to obtain a composition of matter patent. In other instances, because of long drug development timelines and stringent regulatory requirements and review, a significant amount of the patent term (typically twenty years) of the composition of matter patent has already ticked away by the time the product has been approved for marketing. Even though the US Patent Office, in conjunction with the FDA, provides for up to five years of patent term restoration, the restored patent term can still be relatively short. In many cases composition of matter patents may have expired or may not otherwise be available for reasons having nothing to do with the soundness, value, or utility of the underlying drug product.

Notwithstanding whether there is a composition of matter patent, pharmaceutical companies often supplement their patent portfolios with patents covering manufacturing processes and improvements. These patents are sometimes referred to as secondary patents. These patents can relate to more efficient processes or products with improved purity profiles or properties. However, these secondary patents can be more difficult to monitor and subsequently enforce. The reason for this is that the evidence necessary to substantiate a claim of infringement is not as easy to obtain or demonstrate as in the case of a composition of matter patent. Counterfeiting of pharmaceutical products and

infringement of patent processes are multi-billion dollar problems for the pharmaceutical industry. Here is where the technology developed by Dr. Jasper and his company can come to the rescue.

Identifying the Source of Drugs

Dr. Jasper explained how his isotopic fingerprinting technology can differentiate the source of a drug or the process by which it is made. All chemical compounds have distinctive ratios of natural stable isotopes. Thus every batch of a pharmaceutical material has its own highly-specific isotopic fingerprint. The method can be used to identify, track, and classify batches of products. The technology can identify not only the type of chemical processes used in making a drug, but also the identifying information of the specific manufacturing site as well.

This fingerprinting technology provides a means to investigate and determine facts, with the intent to use them in a court of law if necessary. The information obtained from these forensic methods can be solid and overwhelming evidence in a patent infringement lawsuit. Many times it is difficult to monitor and enforce process patents because of the difficulty of finding persuasive evidence of infringement. The reason Dr. Jasper's isotopic evidence can be so persuasive is because it is so sensitive. The technology can measure very small differences in natural isotopic ratios between samples. Because of this sensitivity the method can, with a very high degree of certainty, determine whether two or more samples or processes are the same or different. According to Dr. Jasper, "we can perform very precise analyses on samples that are only a fraction of a milligram." (To put this in perspective, a typical grain of salt weighs less than a milligram.)

In 2005, in a blind study commissioned by the FDA, MIT LLC characterized 26 batches of the pain reliever, naproxen, to determine the product fingerprint or source characteristics for the batches. The FDA wanted to assess the robustness of the fingerprinting method for determining the manufacturing sites for pharmaceutical products. If the method could provide this source information, it would be an important investigative and forensic tool for drug enforcement authorities trying to determine the provenance of a product. For this study, Dr. Jasper and his team determined the ratios of the naturally-occurring carbon and oxygen isotopes for each of the naproxen batches. It turns out Dr. Jasper and his team had correctly determined that the batches had come from six different manufacturing sites from around the world. (See Figure 1.)

Recent Results

As of this writing, Dr. Jasper claims his technology has led to two lawsuits being decided in favor of plaintiffs claiming patent infringement against counterfeiters. Conversely, his technology has also helped a defendant ward off a claim of patent infringement. MIT LLC conducted a study for this defendant comparing the naturally occurring carbon isotope ratios for the defendant's products versus the ratios for a product made by the plaintiff's patented process. The data unequivocally showed that the defendant's product could not have been made by the patented process as alleged by the plaintiff. Based on the data, the defendant was found not guilty of patent infringement. (See Figure 2.)

Results such as these highlight the importance of this fingerprinting technology, particularly to adding value to a company's patent estate. I asked Dr. Jasper what is on the horizon for his company. He explained they are expanding their business development outreach at the same time that they are developing new isotope analysis tools.

Things have evolved a long way from the early 1900s when researchers first postulated the existence of different isotopic forms of the chemical elements. Nature's Fingerprint® has found a unique application of this isotope technology. It is a company to watch, particularly as it continues to add value to and transform the patent portfolios of the pharmaceutical industry.

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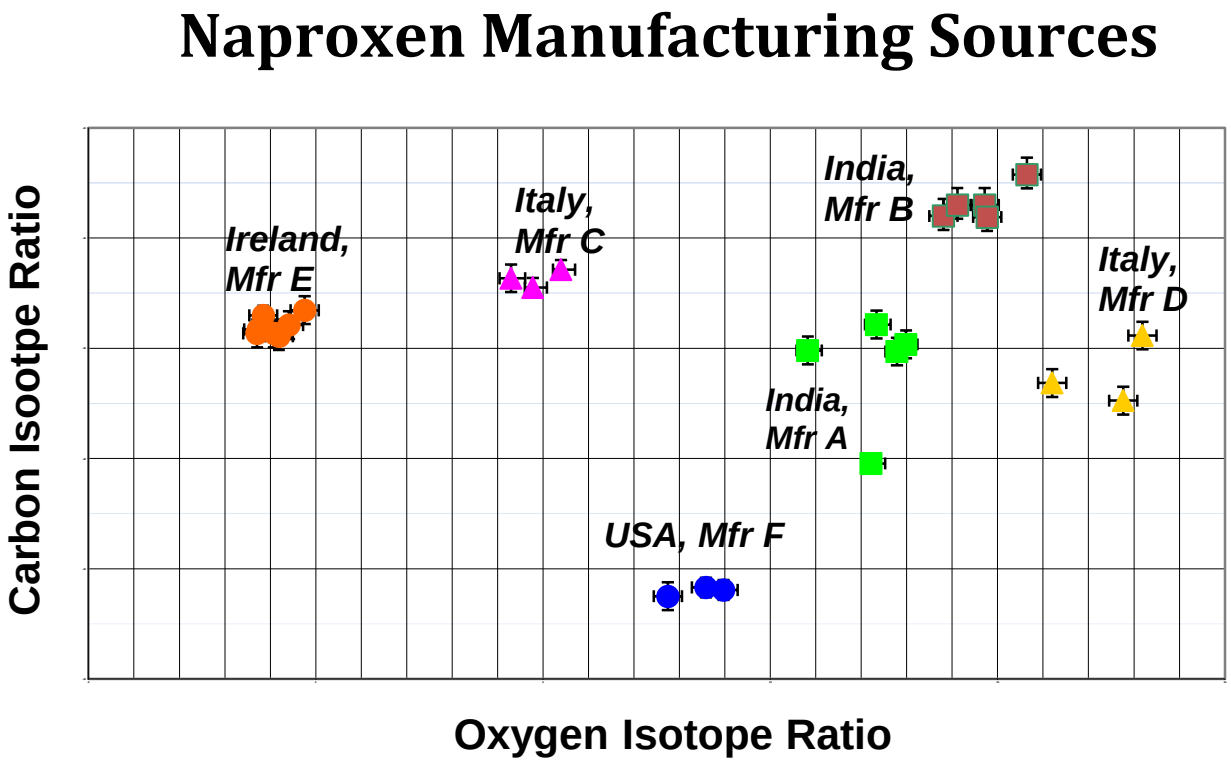

Figure 1. Determination of the Manufacturing Source for Naproxen Samples
MIT LLC's fingerprinting technology was used, in a blind study commissioned by the FDA, to determine the manufacturing source for 26 separate batches of naproxen obtained from various sites around the world. By determining the naturally occurring isotope ratios for the carbon and oxygen isotopes in the samples, as shown in the above graph, Dr. Jasper and his team successfully determined that the 26 batches had come from six different manufacturing sources.

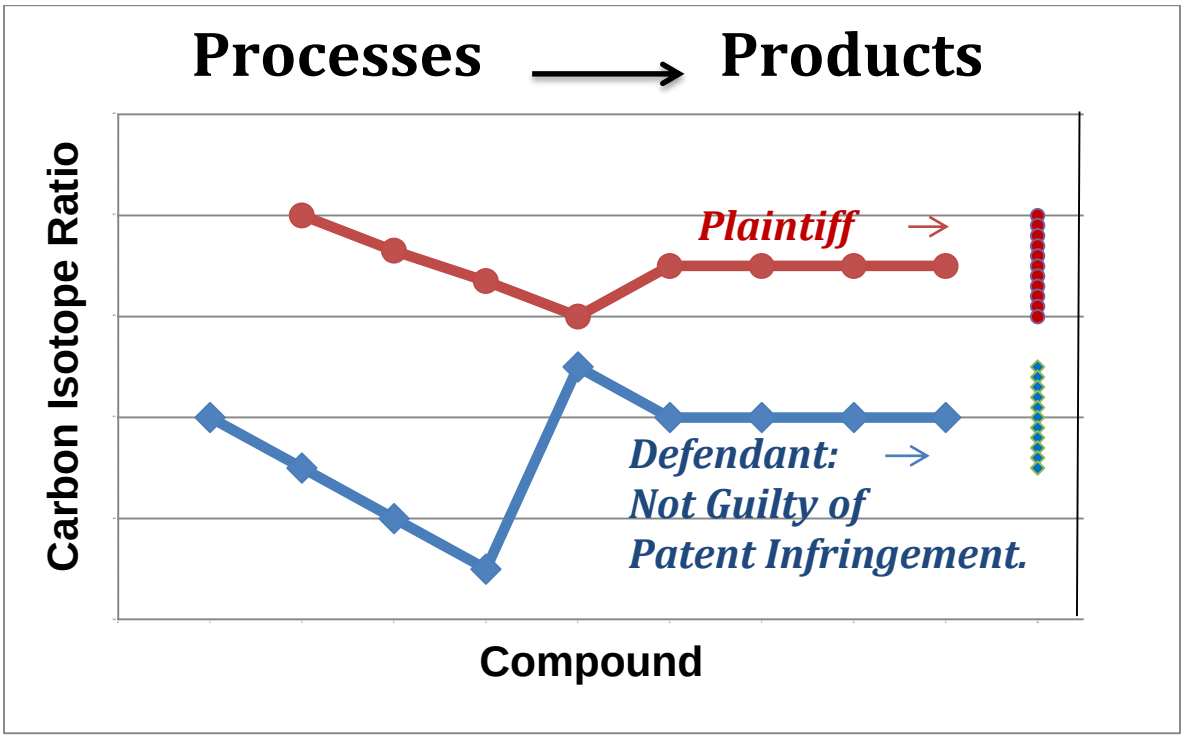

Figure 2. Non-Infringement of a Patented Process
MIT LLC provided data used in the successful defense against a claim of patent infringement. The MIT LLC team conducted a study showing that the naturally occurring carbon isotope ratios in the defendant's products were distinctly different from those of the plaintiff patent holder's process. This difference is dramatically shown from the above graph.