

## Bio/Pharmaceutical Process Patent Protection and Product Characterization via Natural-Abundance Stable Isotopes

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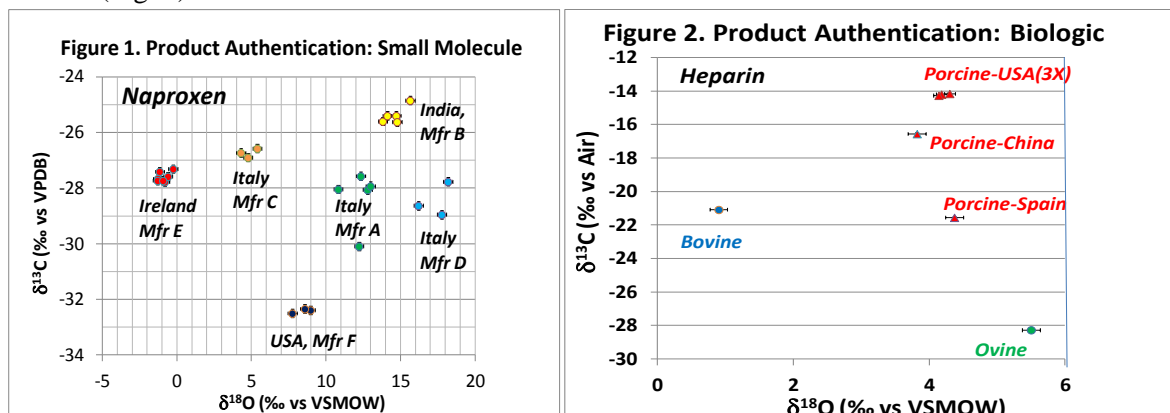
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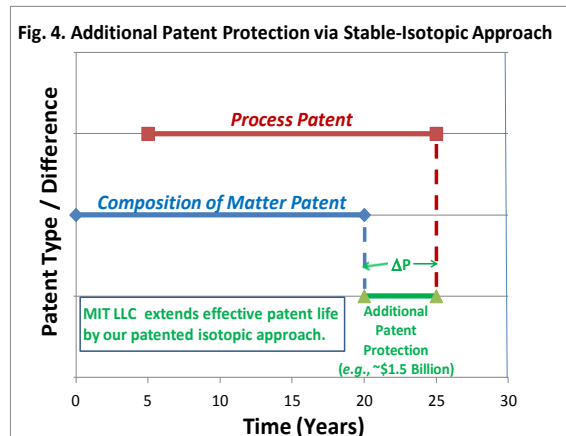
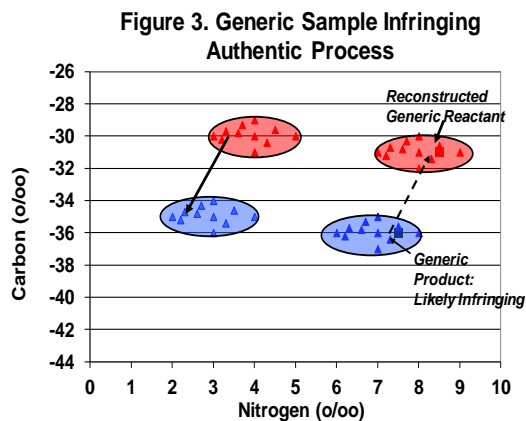
**The Challenges:** Process patent infringement and product mischaracterization of bio/pharmaceutical processes and product represent major economic challenges to the global \$130 billion market.

**What is Nature's Fingerprint® Authentication / MIT LLC?** With more than \$1.5 billion of bio/-pharmaceutical products protected against infringement, the mission of Nature's Fingerprint® is to identify mischaracterized (or counterfeited) bio/pharmaceutical products and cases of process patent infringement for our corporate clients, thereby providing protection to their valuable intellectual-property assets. Nature's Fingerprint® / MIT LLC accomplishes these goals by the analysis of natural-abundance stable isotopes that occur in all bio/pharmaceutical products. As described below, the company provides the Isotopic Pedigree® or IsoPedigree<sup>SM</sup> for products and processes.

**Background.** Naturally-existing tracers ("stable isotopes") exist in all bio/pharmaceutical materials, recording the identity of individual product batches as well as the processes by which they were made. These natural tracers occur in all matter with highly-distinctive "isotopic fingerprints" that can be used to very-highly-specifically authenticate products by Product Authentication. Analogously, the isotopic fingerprinting of a multi-step synthetic sequences leading to a specific product is known as Process Authentication. Nature's Fingerprint® has patents granted and pending in these areas.

**The Product or "Manufacturer's" Fingerprint.** The Product Fingerprint is the combined result of two variables -- the isotopic composition of the starting material and the isotopic characteristics that result from the bio/chemical process is used to convert starting material to finished goods. In 2005, MIT LLC characterized isotopically twenty-six batches of Naproxen in a blind study for the US FDA to determine their product fingerprint or source characteristics. The isotopic compositions of the Naproxen samples clustered into six groups, corresponding to six manufacturers from around the world (Fig. 1). In 2014, MIT LLC and colleagues, isotopically fingerprinted the biologic compound Heparin and were able to differentiate three major sources of the compound (porcine, ovine, and bovine) as well three continental sources (Fig. 2).





**The Process Fingerprint.** The key concept of Process Fingerprinting is illustrated in Figure 3. Knowing isotopic composition of starting material and product allows calculation of the vector (arrow) that represents the multi-step process fingerprint. The same fingerprint results despite multiple sources of starting material having different isotopic compositions.

Isotopic characterization of both the starting material and product allows development a fingerprint for the multi-step process. With this information, infringement can be identified, process patents can be defended, and the product's useful life and revenue stream can be extended beyond the span of the Composition of Matter patent (Figure 4).

### Patents Granted and Pending

Jasper, J. P., Stable isotopic identification and method for identifying products by isotopic composition. (U.S. Patent No.7,323,341).

Jasper, J. P., Tracing processes between precursors and products by utilizing isotopic relationships. (U.S. Patent No. 8,367,414 B2).

Jasper, J. P., Method for continuously monitoring chemical or biological processes. (U.S. patent pending).

Jasper, J. P., Isotopic identification and tracing of biologic products. (U.S. and international patents pending).



(MITLLCsummary2014.2.0.docx)