Exhibit 4

Chapter 800 Restriction in Applications Filed Under 35 U.S.C. 111; Double Patenting

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(C), will be subject to a restriction requirement. Applicants will be required to select one combination for examination. If the selected combination contains ten or fewer sequences, all of the sequences of the combination will be searched. If the selected combination contains more than ten sequences, the combination will be examined following the procedures set forth above for example (B). More specifically, the combination will be searched until one nucleotide sequence is found to be allowable with the examiner choosing the order of search to maximize the identification of an allowable sequence. The identification of any allowable sequence(s) will cause all combinations containing the allowed sequence(s) to be allowed.

In applications containing all three claims set forth in examples (A)-(C), the Office will require restriction of the application to ten sequences for initial examination purposes. Based upon the finding of allowable sequences, claims limited to the allowable sequences as in example (A), all combinations, such as in examples (B) and (C), containing the allowable sequences and any patentably indistinct sequences will be rejoined and allowed.

**>Nonelected claims< requiring any allowable >nucleotide< sequence(s) >should be considered for rejoinder. See MPEP § 821.04<. **

804 Definition of Double Patenting [R-5]

35 U.S.C. 101. Inventions Patentable.

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

35 U.S.C. 121. Divisional Applications.

If two or more independent and distinct inventions are claimed in one application, the Director may require the application to be restricted to one of the inventions. If the other invention is made the subject of a divisional application which complies with the requirements of section 120 of this title it shall be entitled to the benefit of the filing date of the original application. A patent issuing on an application with respect to which a requirement for restriction under this section has been made, or on an application filed as a result of such a requirement, shall not be used as a reference either in the Patent and Trademark Office or in the courts against a divisional application or against the original application or any patent issued on either of them, if the divisional application is filed before the issuance of the patent on the other application. If a divisional application is directed solely to subject matter described and claimed in the original application as filed, the Director may dispense with signing and execution by the inventor. The validity of a patent shall not be questioned for failure of the Director to require the application to be restricted to one invention.

The doctrine of double patenting seeks to prevent the unjustified extension of patent exclusivity beyond the term of a patent. The public policy behind this doctrine is that:

> The public should . . . be able to act on the assumption that upon the expiration of the patent it will be free to use not only the invention claimed in the patent but also modifications or variants which would have been obvious to those of ordinary skill in the art at the time the invention was made, taking into account the skill in the art and prior art other than the invention claimed in the issued patent.

In re Zickendraht, 319 F.2d 225, 232, 138 USPQ 22, 27 (CCPA 1963) (Rich, J., concurring). Double patenting results when the right to exclude granted by a first patent is unjustly extended by the grant of a later issued patent or patents. *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982).

Before consideration can be given to the issue of double patenting, two or more patents or applications must have at least one common inventor and/or be either commonly assigned/owned or non-commonly assigned/owned but subject to a joint research agreement as set forth in 35 U.S.C. 103(c)(2) and (3) pursuant to the CREATE Act (Pub. L. 108-453, 118 Stat. 3596 (2004)). Congress recognized that the amendment to 35 U.S.C. 103(c) would result in situations in which there would be double patenting rejections between applications not owned by the same party (see H.R. Rep. No. 108-425, at 5-6 (2003)). For purposes of a double patenting analysis, the application or patent and the subject matter disqualified under 35 U.S.C. 103(c) as amended by the CREATE Act will be treated as if commonly owned. See also MPEP § 804.03. Since the doctrine of double patenting seeks to avoid unjustly extending patent rights at the expense of the public, the focus of any double patenting analysis necessarily is on the claims in the multiple patents or patent applications involved in the analysis.

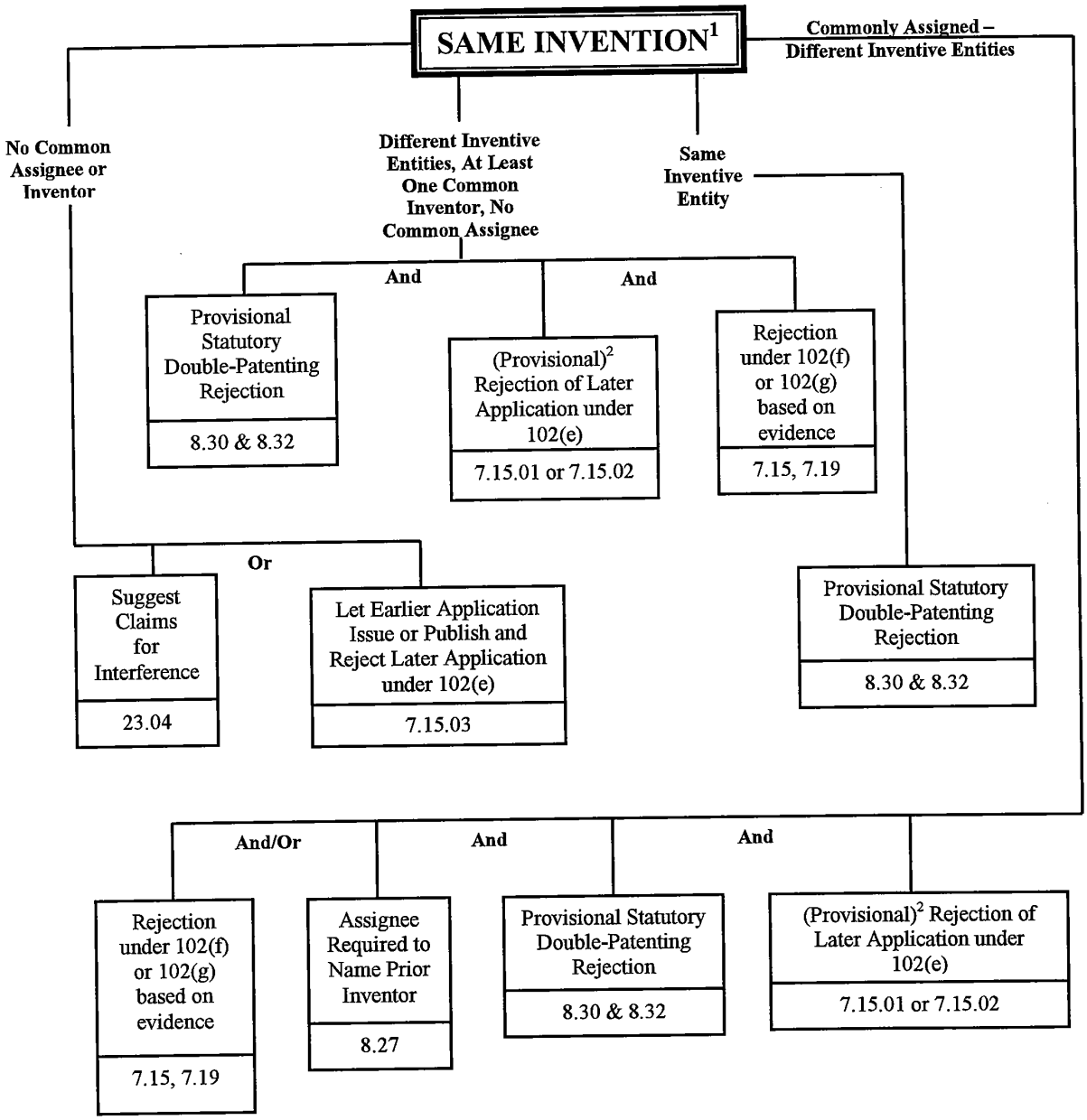
There are generally two types of double patenting rejections. One is the “same invention” type double patenting rejection based on 35 U.S.C. 101 which states in the singular that an inventor “may obtain a patent.” The second is the “nonstatutory-type” double patenting rejection based on a judicially created

doctrine grounded in public policy and which is primarily intended to prevent prolongation of the patent term by prohibiting claims in a second patent not patentably distinguishing from claims in a first patent. Nonstatutory double patenting includes rejections based on either a one-way determination of obviousness or a two-way determination of obviousness. Nonstatutory double patenting could include a rejection which is not the usual "obviousness-type" double patenting rejection. This type of double patenting rejection is rare and is limited to the particular facts of the case. *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968).

Refer to Charts I-A, I-B, II-A, and II-B for an overview of the treatment of applications having conflicting claims (e.g., where a claim in an application is not patentably distinct from a claim in a patent or another application). See MPEP § 2258 for information pertaining to double patenting rejections in reexamination proceedings.

CONFLICTING CLAIMS BETWEEN TWO APPLICATIONS

CHART I-A



[1] The joint research exclusion of 35 U.S.C. 103(c) is not applicable.

[2] Where the application being applied as a reference has NOT been published, the rejection under 102(e) should be provisional.

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