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Measuring Concentration in the Biotechnology R&D Industry: Adjusting for Interfirm Transfer of Genetic Materials

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A new measure of concentration is developed for innovation markets. The new measure accounts for strategic alliances in which one biotechnology firm grants another firm access to its proprietary plant gene constructs. Such alliances are common in biotechnology but are not considered in previous measures. Application of this measure to the plant biotechnology research and development (R&D) industry reveals that concentration is higher and more consistent over time than traditional concentration measures indicate.

Key words: agricultural research, agriculture, biotechnology, concentration, gene constructs, innovation, market structure, R&D.

Although many market-share-based concentration measures exist for product markets, such measures cannot be applied directly to innovative activity for products that have not yet been commercialized. The need for concentration measures and the analysis that accompanies them is readily evident in the biotechnology research and development (R&D) industry. Both biotechnical advances and legal changes have created a situation in which a few companies are positioned to influence the direction of biotechnology R&D and access to biotechnology products (Lesser, 1998; Wolf & Zilberman, 1999). Previous theoretical and empirical studies of R&D industries suggest that an intermediate degree of output-market concentration between monopoly and competition optimizes R&D performance (e.g., Loury, 1979) and so does intellectual property protection that leads to market power (e.g., Segerstrom, 1998). High levels of concentration, though, can lead to suboptimal R&D and innovation levels. In the case of biotechnology industry, concerns about concentration have focused on its impact on the pace of innovation (Brennan, Pray, & Courtmanche, 1999), the distribution of benefits (Falck-Zepeda, Traxler, & Nelson, 2000), the role of the public sector (Klotz-Ingram & Day-Rubinstein, 1999), and appropriate policy (Ward, 2000).

Contemporary empirical analyses of biotechnology industry concentration borrow heavily from traditional concentration measures developed for output markets. Typically, a sales-based four-firm concentration ratio (CR4) is adapted for use in biotechnology by replacing data on product sales with data on R&D activity (the CR4 is the aggregate market share of the four largest firms, usually expressed as a percentage). For example, Brennan, Pray, and Courtmanche (1999) and Oehmke (2001) calculate CR4 type measures for plant biotechnology by replacing market share with the proportion of transgenic field trials conducted by the different firms. That is, their CR4 measure is the proportion of all field trials conducted by the four largest firms (those with the most trials). In essence, this approach to R&D concentration treats each biotechnology firm as an independent entity with no alliances.

In agricultural biotechnology, R&D interfirm alliances are common (James, 1999). These alliances, which may encompass license agreements and subcontracts to utilize technologies, are not accounted for by concentration measures that treat each firm performing field trials as an independent observation. In biotechnology R&D, plant varieties invented by one firm but tested by another company have not been counted toward the share of R&D activity of the inventing company. For example, if Monsanto subcontracted with Stein to field test transgenic soybean varieties, under previous concentration measures this arrangement would appear as independent companies conducting independent research.

In this paper, we consider a plant biotechnology R&D concentration measure that explicitly accounts for ownership of the transgenic constructs. Thus, interfirm alliances or agreements to test a single gene construct are not counted as independent trials. By accounting for alliances, this measure provides a different and potentially more accurate measure of R&D concentration. In the next section, we briefly review transgenic plant biotechnology to explain the role of gene constructs and industry behavior. The third section examines the importance of ownership of the transgenic material. Then we construct an alternative measure of concentration. Finally, we compare the alternative measure to the traditional measure. We find that both measures are use-

ful. The existing measure is best used in measuring concentration in a product market; the new measure, based on the number of independently owned gene constructs, is more useful in examining structure of innovative activity.

Transgenic Plant R&D and Ownership of Transgenic Materials

Transgenic plant varieties are created by taking DNA sequences from organisms—including unrelated plants, bacteria, and viruses—and inserting these sequences into the genome of the desired plant variety. If successful, the resulting transgenic plant possesses economically desirable characteristics (such as herbicide tolerance or insect resistance) relative to existing varieties. The new gene, which is specifically designed to confer these characteristics in typical environments, is referred to as a *gene construct*. The objective of a significant amount of private-sector biotechnology research is primarily to find or create and patent new and economically useful gene constructs.

When the genetic material has been successfully transferred, the innovator field-tests the variety under United States Department of Agriculture Animal Plant and Health Inspection Service (APHIS) guidelines; if the innovator considers the trial successful, it then applies to APHIS for deregulation (Belson, 2000). If APHIS grants deregulated status, then the transgenic variety may be commercialized like any traditional variety, with no further regulation specific to its transgenic status. Once a transgenic variety is deregulated, it can be crossed with other varieties and pass on its genetics without further involvement from APHIS.

All of the deregulated varieties and most (if not all) of the varieties tested in field trials are protected under various types of intellectual property rights. In the United States, the Plant Patent Act of 1930 and the Plant Variety Protection Act of 1970 provide sui generis protection of intellectual property residing in plants. In *Diamond v. Chakabarty*, the US Supreme Court allowed protection of living tissue via utility patents. Ensuing case law extended this protection to genetic material. In particular, ex parte *Hibberd* extended the application of utility patents to novel plant varieties. The upshot is that intellectual property protection for gene constructs and the plants that embody them is quite strong.

The nature of biotechnology and the strong protection of transgenic varieties create some unique conditions that could affect the pace of innovation. In biotechnology, the Schumpeterian idea that the next innovation will make obsolete and replace the last does not always hold. In agricultural biotechnology, the next innovation is likely to "stack" traits upon those developed in the previous innovation. For example, herbicide-tolerant corn may be followed by corn that is both herbicide tolerant and insect resistant. In cases of trait stacking, each succeeding innovation most likely relies on a patent(s) held by the previous innovator(s)—for example, the patents related to herbicide tolerance. As long as biotechnology advances by stacking additional traits onto existing varieties, there could be an issue of access to the intellectual property, which in turn could act as a barrier to R&D and innovation.

It is theoretically possible, of course, to "leapfrog" existing patents and commercialized traits. It is unclear, however, that a meaningful number of new traits that could make some of the commercially successful first generation traits obsolete are currently forthcoming.

It is also theoretically possible to "invent around" existing patents—for example, by coming up with an alternative, unpatented genetic form of glyphosate (Roundup) tolerance. This is certainly no easy fit. For instance, it is true that many companies (most notably Calgene) had worked on glyphosate tolerance and discovered and patented genetic material that impedes one or more of the chemical pathways by which glyphosate works. These genes did not confer sufficient tolerance in plants, however. Eventually, Monsanto found the gene for glyphosate resistance in the waste sludge outside the chemical factory that produced Roundup. Monsanto's glyphosate-resistant gene performed its function in the plant cell and proved to tolerate Roundup far better than any gene the scientists had created in the laboratory (Charles, 2002).

An innovator may also wish to stack a new gene atop a competitive trait (e.g., a gene that confers resistance to a competitive herbicide other than Roundup). However, herbicides with much smaller market share imply smaller profits for the new innovation. Hence, alternative herbicides are poor (economic) substitutes for Roundup, and consequently other herbicide-tolerant varieties are not good substitutes for Roundup Ready varieties (Carpenter & Gianessi, 1999). The end result is that there is again a negative effect on the incentive to innovate.

Inventing around *Bacillus thuringeniesis* (Bt) toxin might also be quite difficult. There are 98 different types of Bt holotype toxins (Crickmore, 2004), but only six different Bt types in crops that the USDA has deregulated for commercialization: four in crops commercialized by Monsanto, one by Dow, and one by Aventis. The

CryIA(b) used by Monsanto was also used in varieties deregulated in 1995 by Ciba-Geigy and Northrup King (APHIS, 2004), now parts of Syngenta. However, the same protein isolated from different Bt strains can vary slightly in its amino acid sequence (e.g., by one or two residues) and can have dramatic effects on insecticidal activity (DeWald, 1995). Different Bt proteins target different insect orders and species, so that there may be a very limited substitutability of one Bt construct for another.

Even if "leapfrogging" and "inventing around" are likely to occur, they almost certainly entail economic costs. Thus, the profit incentive to invest in R&D is reduced, once again acting to reduce the pace of inventive activity. Thus, the issue of the number of independent firms developing independently owned gene constructs is important to the future of biotechnology innovation. The existence of a large number of gene constructs under development and testing by multiple independent firms is likely an indication that the market for these gene constructs will be competitive. A small number of gene constructs—no matter how many firms are testing them—could lead to excessive concentration and limited innovative activity.

The number of different gene constructs under development by independent firms is ultimately an empirical issue. By adapting existing concentration measures to account for the possibly limited number of gene constructs under development, we propose a new concentration measure that provides new information on the structure of the transgenic plant R&D industry.

Constructing A Gene-Construct-Based Concentration Measure

We know that in concentrated industries, the threat of entry by competitors is often sufficient to generate competitive outcomes (Baumol, Panzar, & Willig, 1998). In biotechnology R&D, the need for current innovations often to rely on previously patented gene constructs may constitute a barrier that can negate the threat of entry into either the R&D market or the product market. Concentration measures based only on the number of firms performing R&D fail to capture the important intellectual property issue of access to the previous trait(s). Thus, examination of concentration, as measured by ownership of gene constructs, can provide new information on the structure of the plant biotechnology R&D industry.

Upon recognizing the importance of gene constructs, our construction of a CR4 type measure is straightforward. We count the number of trials of each type of gene construct (e.g., any modified gene containing the genetic code for phosphinothricin acetyltransferase) oriented towards the specified varietal characteristic (e.g., herbicide tolerance). These numbers are summed to arrive at a total number of trials for that varietal characteristic, which serves as the denominator in the concentration ratio. The numerator is constructed by summing the numbers of field trials oriented towards the specified varietal characteristics of the four most frequently used gene constructs. Dividing the denominator into the numerator gives a ratio from zero to 100% that is interpreted analogously to the CR4: a value of 100% indicates a pure monopoly, and the smaller the value, the greater the association with a competitive market structure. We refer to this measure as the *GR4* (GR for gene-related).

We apply this measure using data from APHIS on the deregulations and transgenic field trials (the same data used by Brennan, Pray, & Courtmanche, 1999, and Oehmke, 2001, *inter alia*). We apply this measure both to aggregate trials and deregulations through time and to annual numbers of trials.

An issue with any field-trial-based measure arises in that transgenic field trials may serve the dual role of validating the research and meeting regulatory requirements.[1] In particular, in order for a transgenic crop to be used commercially, it must be "deregulated" by the USDA—that is, the phenotype must be found to be substantially the same as the nontransgenic crop. Because the phenotype is the product of the genotype and the environment, companies applying for deregulation may have to increase the number of field trials in order to show that the phenotype is substantially the same as the nontransgenic crop in a wide variety of environments in which the crop may be grown.[2] This means that if a firm is about to request deregulation, it may engage in a

1. *This issue applies to any analysis based on numbers of transgenic field trials—whether a concentration ratio or some other measure. Brennan, Pray, and Courtmanche (1999) were the first to adapt a standard output-market concentration measure (the Herfindahl index) for use with transgenic field trials. Oehmke (2001) used a CR4 index with transgenic field trials. Fulton and Giannakas (2001) summarized evidence on biotechnology concentration from a number of different concentration levels and from both output and innovation markets*
2. *Other companies may systematically test in a wide variety of environments or may use multilocation trials to meet this need without affecting the number of trials as measured by APHIS.*

larger than normal number of field trials, leading to a higher concentration ratio in that year. Hence, field-trial-based concentration measures can be influenced by the stage of the biotechnology innovation cycle (e.g., Kalaitzandonakes & Bjornson, 1997).

The response to this issue depends on the researcher's perspective. If the researcher believes a priori that this is a problem, then a straightforward solution is to quantify the effect of the deregulation request and adjust the data, analogously to seasonal adjustment of time-series data. The magnitude of the adjustment will depend on the quantification technique and the case examined.[3] An alternative perspective is that this economic construct simply places greater weight on those genetic constructs that are more likely to be commercialized. This weighting scheme has some advantages. First, the weights are endogenously determined by the companies' perceptions about their product and whether it can be successfully deregulated and commercialized, so that they contain information. Second, the weighted measure is expected to be a better predictor of transgenic seed market concentration, in the sense that the weighted measure relies more heavily on varieties that are closer to being sold in the marketplace. We adopt the latter perspective in this paper.

Applying the GR4 Measure

APHIS requests information on gene constructs in every application for permission to conduct field trials (environmental releases). Unfortunately, in the publicly available data set, a number of the constructs are listed as confidential business information. However, closely related information is the phenotype of the tested variety. For example, the corn phenotype of glyphosate tolerance can be readily associated with one of two gene constructs conveying this tolerance in standard farming environments.[4] Information on phenotype is publicly available for 99% of the population. We construct the GR4 concentration measures using the phenotype availability.

The proportion of field trials in the two or four most popular phenotype categories through the end of 2000 provides a concentration measure (GR4). The phenotype-based GR4 was uniformly more concentrated than the traditional firm-based CR4 in these markets (Figure 1). For herbicide-tolerant corn, 96% of the field trials were to confer one of four phenotypes.[5] In herbicide tolerance in soybeans, 86% of the trials also conferred one of these phenotypes. For cotton, the four primary herbicide-tolerant phenotypes accounted for 81% of field trials. With respect to insect-resistant corn phenotypes, four phenotypes accounted for 99% of transgenic insect-resistant corn trials. In cotton, 182 of the 183 transgenic insect-resistance trials were one of two phenotypes leading to a 100% concentration ratio.

The traditional CR4s are smaller in every case than the GR4s. This is intuitively plausible: Using a concentration measure designed to include alliances based on shared genetic material shows higher concentration than measures that ignore such alliances.

Annual comparisons of the different concentration measures for herbicide tolerant crops and insect resistant crops show even greater discrepancies. For all herbicide-tolerant crops, the GR4 measure varies from 85% to 99% over the past ten years (Figure 2). For comparison, we reproduce the CR4 measure from Oehmke (2001) based on number of field trials by firm. The CR4 number is lower than the GR4 measure in every year and is substantially more volatile over the period.

The firm-based CR4 measure suggests a cycle of momentary monopoly power that provides incentive for entrepreneurial firms to enter and pursue innovative activity that lowers the concentration. In contrast, the GR4 measure suggests that concentration is uniformly high and perhaps increasing.

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3. For example, a simple regression of trials on the number of deregulations in the following year generates a coefficient of 38 (p-value of 0.006). An OLS regression of trials on crop and time dummies (a fixed-effect situation) and number of deregulations in the following year generates a coefficient on deregulations of 15 (p-value = 0.13); both the coefficient value and the statistical significance depend on the regression model chosen. Taking the value of 15 as fact, for tomatoes in 1995, the GR4 changes from 0.58 to 0.48; for corn in 1997, the GR4 changes from 0.73 to 0.72. The absolute and relative magnitudes of the change also depend on the case selected.

4. Similarly, the gene constructs for lepidopteran resistance typically use a CryI class protein from Bt, for coleopteran resistance CryII class proteins are used, and so forth.

5. For HT corn and soybeans, the phenotypes were glyphosate tolerance, phosphinothricin tolerance or resistance, imidaxazole tolerance, and imidaxazolinone tolerance. For cotton, the four primary herbicide-tolerant phenotypes are glyphosate tolerance, phosphinothricin tolerance, bromoxynil tolerance and 2,4-D tolerance. The most common insect-resistant corn phenotypes are coleopteran resistance, earworm resistance, resistance to the European corn borer, and lepidopteran resistance. For cotton, 182 of the 183 transgenic insect-resistance trials were for coleopteran or lepidopteran resistance (information is missing for the other trial).

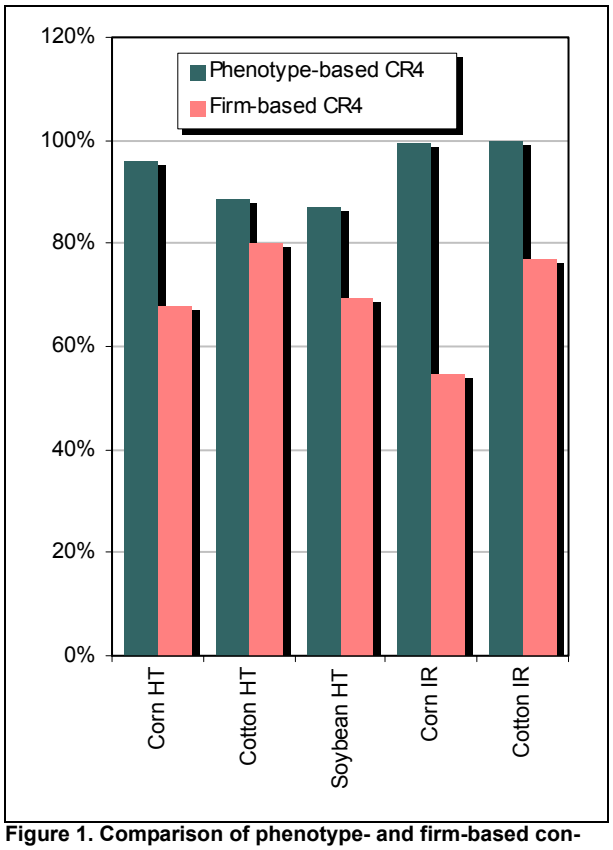

Figure 1. Comparison of phenotype- and firm-based concentration ratios.

For transgenic insect resistance, the GR4 also shows higher and more stable concentration than does the firm-based measure (Figure 3). The GR4 measure ranges from 95% to 99%; the CR4 ranges from 48% to 92%. As with the herbicide-tolerance measure, the CR4 measure shows a period of high concentration in 1994 (and again in 2000) followed by a period of rapidly decreasing concentration. In contrast, the GR4 measure shows concentration measures throughout the sample period that are high.

How Concentrated is the Plant Biotechnology Industry?

We distinguish between the R&D industry (which is in the business of developing gene constructs) and the transgenic seed industry (which is in the business of selling seed for commercialized transgenic plant varieties). We first apply the GR4 measure to the transgenic seed industry and then examine the correspondence between this measure and the GR4 and CR4 measures applied to the R&D industry.

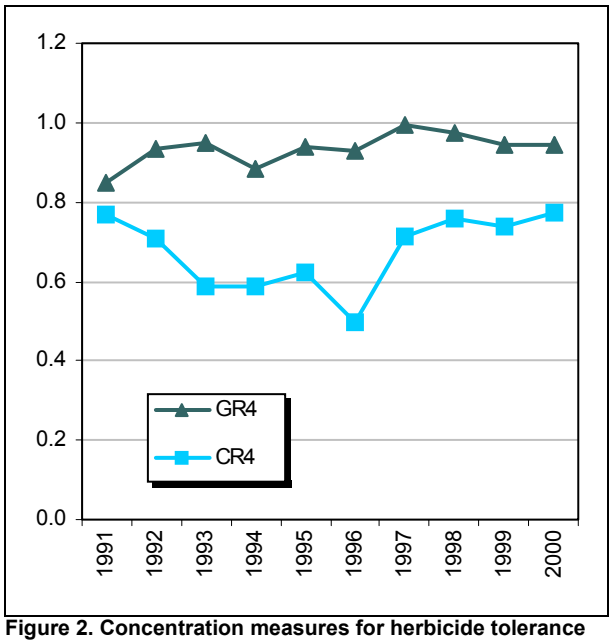

Figure 2. Concentration measures for herbicide tolerance R&D, 1990-2000.

The transgenic seed industry is rather concentrated. In 1999, there were only four firms with significant revenue from sales of transgenic plant seed or biotechnology trait rights (Monsanto, 1999).[6] Only eight firms have ever successfully deregulated a herbicide-tolerant (HT) variety of any crop (based on APHIS data), and only four of these currently exist as firms with independent technologies. For insect resistance only seven firms have successfully deregulated, and only four of these are still operating independently. For product quality, only seven firms have successfully deregulated, and only three still exist independently.

The three crops with the largest area planted to transgenic varieties are corn, cotton, and soybeans. Through the end of 2000, nine corn varieties involving two gene constructs were deregulated for five firms (Figure 4). However, one innovating firm was purchased (Monsanto purchased Calgene), so that there are only three currently existing firms with herbicide-tolerant corn available. For herbicide-tolerant cotton, four varieties involving three gene constructs were deregulated for three firms, which are still distinct firms (the fourth was

6. *Although it is true that only four seed firms have had significant sales from proprietary biotechnology traits, a large number of small regional and medium size national seed firms in the United States and elsewhere have secured licenses and have commercialized key biotechnology traits through their germplasm.*

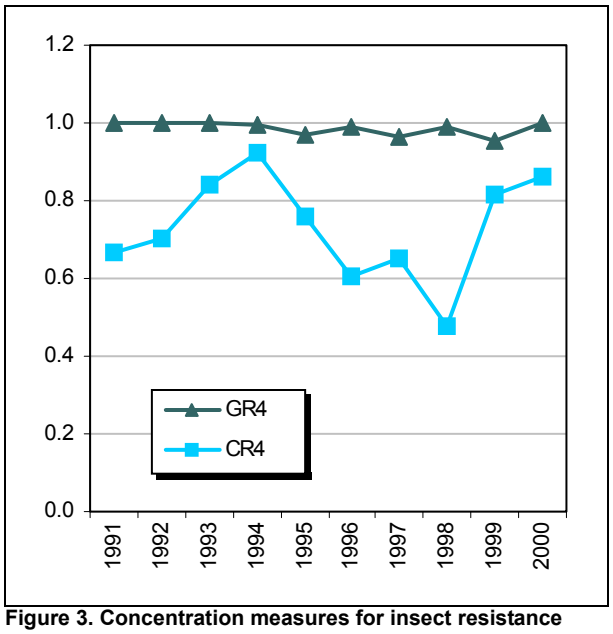

Figure 3. Concentration measures for insect resistance R&D, 1990-2000.

Calgene). Four herbicide-tolerant soybean varieties involving two gene constructs were deregulated for two firms; each is still operating. Eight insect-resistant corn varieties involving four gene constructs were deregulated. Six firms were involved in these innovations, of which two were acquired. Two cotton varieties involving one gene construct were deregulated by two firms; one of these firms bought the other.

At the end of 2000, there was no difference between a firm-based concentration measure and a gene-construct based measure. With no more than four firms or gene constructs in any category, either the CR4 or GR4 concentration measures equaled 100%.

A useful comparison is of concentration measures at the field-trial level with concentration measures at the deregulation and output-market levels. The gene-based concentration ratio at the field-trial stage is in every available case closer to the output-market CR4 than is the firm-based concentration measure at the field-trial stage. That is, in Figures 2 and 3 we showed that the GR4 measure is more stable and in every available case greater than the adapted (trial-level) CR4 measure; therefore, the GR4 measure is always closer to the seed-market concentration ratio. An intriguing question is whether the GR4 measure is a better predictor of future seed-market concentration, but the data are not yet available to make this a meaningful empirical question.

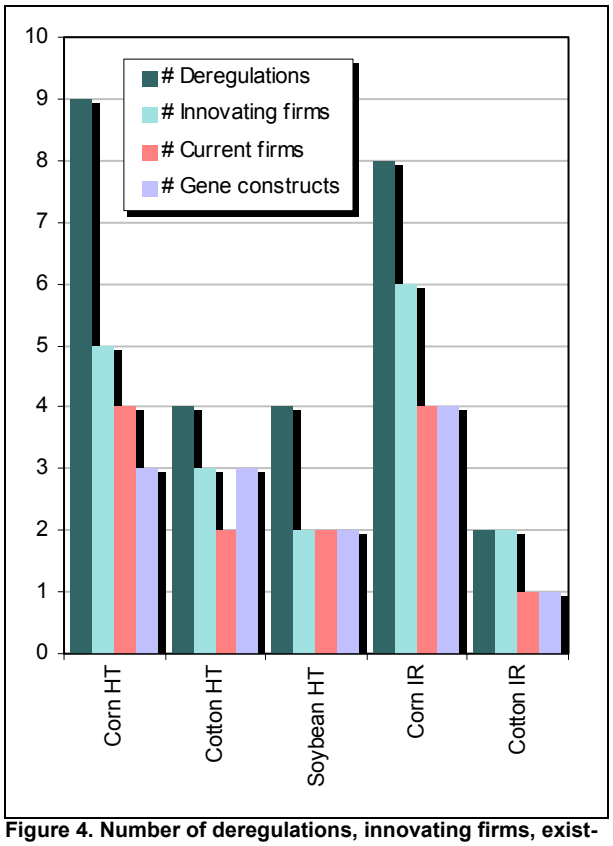

Figure 4. Number of deregulations, innovating firms, existing firms, and gene constructs for corrn, cotton, and soybeans through 2000.

Conclusions and Implications

Accounting for interfirm sharing of plant biotechnology gene constructs leads to a different, and perhaps more complete, picture of R&D concentration levels than those found with firm-based measures. Concentration at the transgenic field-trial stage of the R&D-to-commercialization continuum is much higher and more stable when calculated with the GR4 measure. There is little discrepancy between the two measures at the deregulation stage that is close to commercialization. Because sharing of gene constructs is most important at the R&D stage, the greater discrepancy between measures at the field-trial stage is intuitively plausible.

Even with this new measure of concentration to consider, firm-based measures are informative. Indeed, many of the interesting industry evolution issues center around changes in the number and size of firms over time, especially in output markets. However, especially with respect to the R&D industry, a gene-related measure provides important new insights. This is true even with respect to industry evolution.

Using a concentration ratio based on gene constructs could shed light on the important question of future market competition. For instance, if a group of firms conducts research on herbicide tolerance based on a single gene construct, the owner of that construct can reasonably be expected to generate royalties from every sale in that output market, providing at least a degree of monopoly power. However, if multiple gene constructs are the foundation for this research, then intuitively there is a greater likelihood that multiple independent firms will provide a degree of competition in the output market (or at least the threat of entry). Thus, examination of concentration measured by ownership of gene constructs provides useful information on the structure of the plant biotechnology R&D industry.

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