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A META-ANALYSIS OF GM CROPS REGULATORY APPROVAL COSTS

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ABSTRACT

Concerns over the effects on human and animal health from consumption of genetically modified food crops, as well as about potential impacts on the wider environment, have divided public opinion over the merits of using the technology. One consequence is that governments have traditionally been very cautious about approving GM crops for cultivation and consumption. A concomitant effect is that the costs involved (and time spent) in achieving regulatory approval for the introduction of a GM crop have risen. This study examines the evidence on the absolute and relative costs of gaining regulatory compliance, first by surveying the literature to gain some insights into the scale and range of costs. The data reveals significant differences which are then unpacked using meta-analysis. The analysis reveals that product attributes, market context and technical aspects of measurement all have significant effects on the costs of regulatory approval.

KEYWORDS: GM crops, regulatory costs, meta-analysis

1. INTRODUCTION

The introduction of transgenic technology into agriculture in the 1980s triggered significant regulatory reform. After considerable debate and investigation, the US and eventually most initial developers and adopters of genetically modified (GM) crops adopted new guidelines and procedures for evaluating the safety and efficacy of crops using this new technology. The net effect was that proponents of new crop varieties embodying GM traits were required to undertake more intensive pre-market assessment which would be adjudicated by national regulators wherever the varieties were intended to be produced or consumed—previously most crop varieties developed through traditional plant breeding methods were initially (and often only) assessed in the country where the variety was developed and first commercialized. By 2013, most countries had enacted some form of regulation or policy directly targeted at GM crops, whether they are intended to be planted, consumed, processed or traded. This policy change imposes both real and opportunity costs on both the technology and the economy.

This paper assesses the scale and scope of the use of GM technologies and the measurable costs of regulating them at the product and market level. In the first instance, we examine the

nature of the regulatory system directed at GM crops and then examine the evidence about costs and impacts presented in a range of studies. These studies are then assessed using meta-analysis to identify potential causes for differential costs (or at least for differential estimates). Finally, the paper puts these costs into context of the real and potential impact of the technology on global food security and economic welfare.

2. BACKGROUND

In 1996 the first significant area of crops containing GM traits were planted (1.7 million hectares). Since then there has been a dramatic increase in plantings; by 2012, the global planted area reached 170 million hectares (ISAAA 2013). GM traits have largely been adopted in four main crops—canola, corn, cotton and soybeans—although small areas of GM crops in sugar beet (adopted in the USA and Canada since 2008), papaya (in the USA since 1999 and China since 2008) and squash (in the USA since 2004) have also been planted. In 2012, 28 countries planted GM crops, more than half developing nations. Six countries accounted for 92% of total production: US, Brazil, Argentina, Canada, India and China (in declining order of area). Two traits dominate: herbicide tolerant (HT) crops account for 65% of the total area planted to GM crops while insect resistant (IR) crops account for 35% of global plantings; a rising portion of the area involves stacked HT and IR traits. GM seeds account for 70% of the global soybean acreage, 52% for cotton, 26% for corn and 20% for canola. In those countries adopting GM varieties, GM seed market share has risen above 80% in those crops. GM crops have also been pro-trade, in that adoption and production is concentrated in leading export nations. Brookes (forthcoming) estimates that biotechnology producers account for between 72% of cotton and 95% of soybean global trade.

While there has been significant study of the underlying regulatory regimes in the divergent countries (for example Isaac 2002, Skogstad 2010 and Doern and Prince 2012), that is not the focus of this paper. The main point to draw from that literature is that there are fundamental differences of approach and impact, which contributes to asynchronous reviews and approvals. In 19 countries that had examined and approved at least one of the 144 events proposed by 2011, the average country had undertaken reviews on only about 5 of the 16 species under investigation and completed environmental reviews on 12% of the possible cases and food safety audits on 27% (Phillips 2011). No single country reviewed and recorded positive approvals for all of the 144

events proposed as of 2011. The highest rates of positive review were in Canada and the US, two of the largest producers and exporters of GM crops, and Japan, a key importer of foodstuffs with GM traits. The low level of successful review for environmental release reflects the politics of the adopting countries while the somewhat higher percentage of completed food reviews reflects the reality that much of the international trade now includes GM elements.

One aspect to keep in mind is that companies make their own decisions about where and when to seek approval for commercialization. Soybeans and maize/corn have the highest penetration rates, averaging around 10% of the total countries producing those crops. Nevertheless, those countries adopting GM varieties account for an estimated 73% of global soybean area and 30% of global maize/corn area. While one might interpret incomplete adoption as reflecting the unwillingness of countries to accept GM technologies, in many cases it is simply a business decision based.

Truncated adoption can be the result of two separate decisions. Many interpret the limited regulatory acceptance of GM crops as a judgment of regulators—some assume that stalled introduction are because companies have failed to satisfy the regulators of the health and environmental safety of their products. In fact, in many cases proponents are simply waiting for regulators to make their judgments. Few if any products have been explicitly rejected for health or environmental safety reasons by any regulator anywhere. What appears to be happening is that many proponents have simply not applied for regulatory assessment in small markets. In many cases it is simply a business decision based on the expectation that there would not be adequate revenues for the technology owners to justify the investments in acquiring regulatory compliance and developing a local supply chain. A number of tentative estimates of the costs of regulatory compliance in developing countries suggests the upfront cost per country have ranged from US$500,000 to US$5 million for the first GM event in a species and taken from 2-7 years to complete, with subsequent GM traits in the same crop being less expensive and somewhat more timely (Kalaitzandonakes, Alston and Bradford 2007; Pray, Bengali and Ramaswami 2005; Pray et al. 2006; Bayer, Norton and Falck-Zepeda 2010). To give you a sense of the problem, assuming a biotechnology company could generate free cash flow of US$10 per hectare planted (which would depend critically on the structure of local intellectual property laws and the structure of the local seed industry) and they got above average farmer adoption, there are at least 40 countries producing maize/corn where it is unlikely for a biotechnology company to recoup even the lowest

likely regulatory costs within 10 years of starting the process. Given there would also be extra development costs to backcross their proprietary traits into cultivars appropriate for those markets, the number of unprofitable markets is probably higher. Few companies are willing to take such unreasonable commercial risks with their scarce capital.

This paper assesses the primary and secondary evidence that delimits the scale and scope of regulatory costs and uses meta-analysis to untangle the drivers of differential estimates by product and market.

3. META-ANALYSIS

The practice of meta-analysis has been developed and applied to a number of subject areas in recent years. Meta-analysis is essentially an analysis of analyses (Hedges and Olkin 1985). The basic approach is to aggregate research findings statistically and calculate a set of explicit or implicit weights for the key factors underlying the findings. A more traditional approach to surveying the evidence would involve narrative reviews and tables of a selection of studies (as is presented in section 4). The terminology of meta-analysis is often credited to the Cochrane Collaboration (http://www.cochrane.org/) which in 1993 introduced multivariate regression to examine the impact of moderator variables on study effect size using regression-based techniques. The goal is to combine the results of two or more separate studies to generate weighted averages of moderator effects on the results in order to increase explanatory power, answer questions not posed by individual studies and settle controversies arising from conflicting claims.

In the economic disciplines, meta-analysis has been applied and used in a range of areas (called instrumental variables), including for returns to agricultural research, environmental evaluation, firm structure and strategy and their impact on innovation and wealth creation, consumer valuation, industrial structure and risk tolerance, and the statistical value of a life (Table 1). In each case, analysts identify an area of substantial research that has generated a diversity of empirical results for an instrumental variable, agglomerate a set of representative estimates (often the number of estimates is greater than the number of studies as authors investigate different specifications and simulations) and identify a set of 'moderators' that may help to explain the diversity of estimates of the instrumental variables. All of these studies use multiple regression techniques to meta-analyze the effect of key factors on the estimate of the instrumental variable.

Table 1: Representative meta-analyses				
Study	Topic	Studies	Observations	Moderators
Alston et al. 2000	Returns to agricultural R&D	294	1858	46
Brouwer et al. 1999	Wetland contingent evaluation	30	103	30
Camison-Zornoza et al 2004	Organizational size and impact on innovation	53	57	25
Datta, Pinches and Narayanan 1992	Factors influencing wealth creating from mergers and acquisitions	41	409	13
Lusk et al. 2005	GM food valuations	25	57	16
Marra and Schurle 1994	Farm level risk and farm size	731	2193	6
Mulatu et al. 2003.	Impact of environmental regulation on international trade	13	691	22
Viscusi and Aldy 2002	Value of a statistical life	49	49	27

While meta-analysis has been adapted and adopted by regulators for use inside the system (e.g. to assess and examine a body of empirical studies of epidemiological or environmental impacts), so far no one has used it to assess the system itself. Executive Order 12866 on Economic Analysis of Federal Regulations (OMB, 1996) offers a cautious endorsement to meta-analysis, noting that combining data or results from a number of different studies can allow one to re-estimate key model parameters, thereby improving confidence in the parameter estimates or alternatively use parameter estimates (e.g. elasticities of supply and demand or implicit values of mortality risk reduction) from different studies as data points to analyze variations as functions of potential causal factors. The Order cautions that meta-analysis must be used carefully, ensuring that the data used are comparable, that appropriate statistical methods are used and that the analysis is undertaken only on studies that measure comparable independent and dependent variables. This signpost is used to guide our choice of studies to include in our analysis.

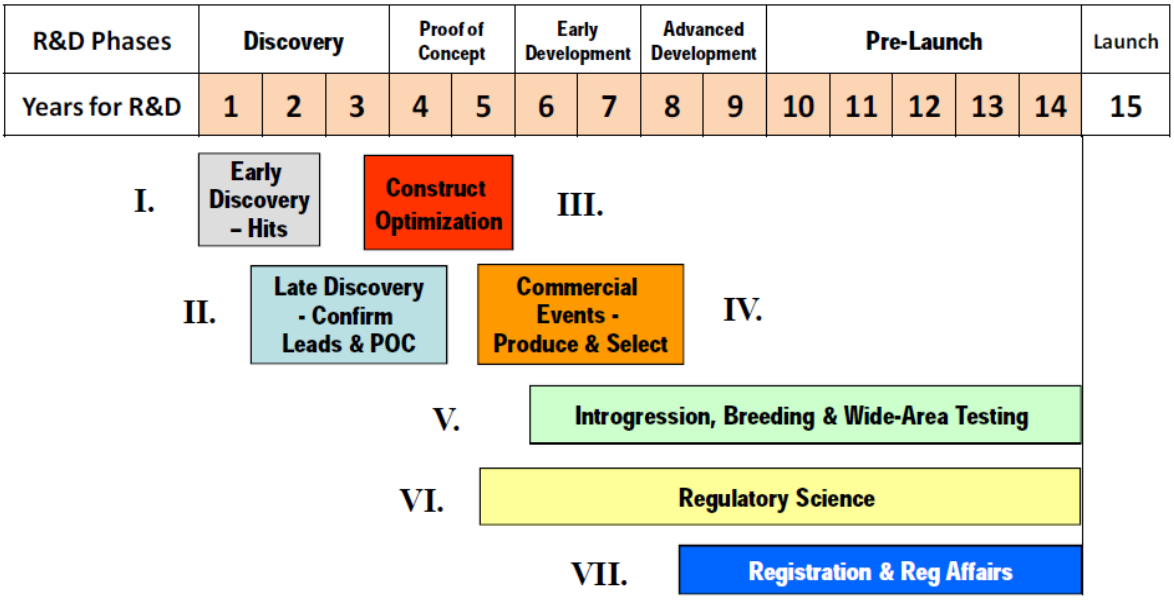
4. THE DATA

The basic challenge in defining the scope of our study is that the costs of full regulatory approval of a biotech crop are not publicly available (and may not actually exist anywhere). At root of the problem is that full information regarding private approval costs have been closely guarded by biotech developers (Kalaitzandonakes, Alston and Bradford 2007). Firms seem to believe that the evidence of their capacity to efficiently and effectively complete the regulatory process is a core competency and hence a proprietary asset that, if more fully disclosed, might be reverse engineered and raise competition in this highly oligopolized market.

Three types of cost analyses have been undertaken so far that have produced an extreme range of estimates of the costs of regulation. A number of economists have worked to construct estimates of the direct cash costs for proponents and regulators of completing the regulatory review of new products, largely based on data gathered from regulators, a few firms and a number of public sector scientists. A subset of economists have looked at regulation as a structural barrier, largely drawing on assumptions about the direct cash costs of regulatory compliance to calculate the opportunity costs of the current regulatory structure. Meanwhile, the big six agricultural biotechnology companies commissioned a study of their all-in costs of bringing a product to market. Given the diversity of approaches, it should not be any surprise that the estimates range widely. Studies peg the cash cost of compliance as low as US$73K for a single event in a single market to as high as US$35 million for cultivation approval in two countries and import approvals in five markets (what the industry asserts is the norm for full introduction of a major crop trait). Meanwhile, the all-in opportunity cost of developing and introducing a trait is estimated to be more than US$130 million, with the dead-weight opportunity cost of regulatory delay adding at least as much to the regulatory burden for firms and the market.

As with many public policy issues, the devil is in the details. The main difference in the estimates can be found by examining what is included and excluded. Phillips McDougall (2011) offered a timeline for the development of a new GM variety, positing that the approximate 15 year research, development and commercialization process involves up to seven interconnected stages, only two of which many would explicitly call regulatory compliance: regulatory science (VI) and registration and regulatory affairs (VII). Nevertheless, the earlier stages of discovery, construct optimization, commercial event selection, introgression and wide-area testing each provides some of the scientific evidence that are explicit inputs to the regulatory process. Comparing and contrasting the different estimates requires knowing what is included and how it is calculated.

Figure 1: The research, development, regulatory and commercial pathway
(source: Phillips McDougall 2011)



In order to be comprehensive, a literature survey was conducted to collect available studies on regulatory approval costs. The collection of literature involved a keyword search of "GMO" and "regulatory costs" in the databases of Thomson Reuters' Web of Science, Research in Agricultural and Applied Economics (AgEcon-Search), AgBioForum, Google Scholar, BEcon and Repec. Other literature (often called the grey market) included conference presentations, policy briefs and a consultancy report on costs in the EU and the US. The literature search was limited to English publications.

The survey identified more than a dozen articles and reports that offer more than 70 estimates of cost of regulatory approval in 16 countries (Argentina, Australia, Brazil, Canada, China, Costa Rica, European Union, India, Indonesia Japan, Kenya, Korea, Philippines, South Africa, Taiwan and the United States) involving a dozen crops and more than 10 different genetic constructs. These studies offer three complementary but substantially different estimates of the cost of regulation. Firstly, a core group of economists has constructed direct cost estimates of regulatory compliance incurred by both proponents and regulators for single events in single markets. Secondly, a number of welfare economists have estimated the opportunity costs of the regulatory process, which includes both the out-of-pocket expenses for both parties and the

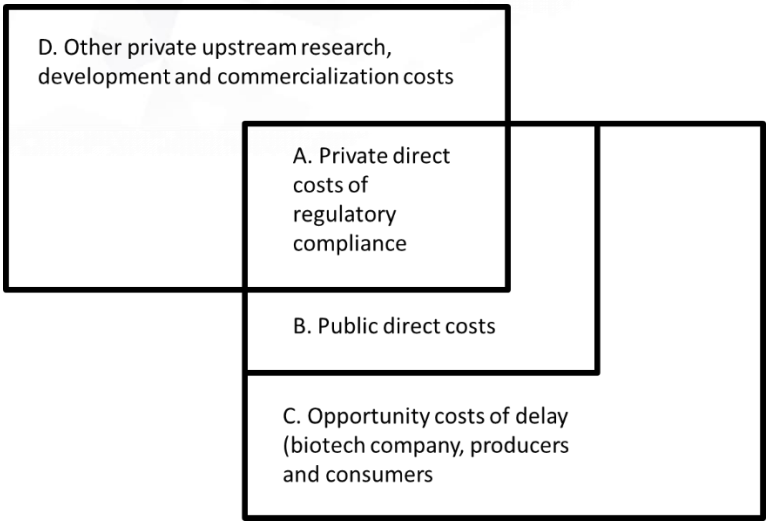
imputed expense of delays in commercialization, both for the proponent and for general social welfare. Thirdly, industry has constructed a set of private costs incurred throughout the discovery and commercialization process, attributing some but not all to the burden of regulatory compliance. As one would expect, the estimates overlap but the means of the estimates differ by at least one order of magnitude due to the underlying assumptions and breadth of the methods (Table 2).

Table 2: A concordance of included and excluded variable in cost estimates

	Costs constructed by economists	Economic welfare analysis	Costs constructed by industry
Example	Kalaitzandonakes, Alston and Bradford 2007	Bayer, Norton & Falck-Zepeda 2010	Phillips McDougall 2011
Total discovery cost	Not included	Not included	Private direct costs calculated; some undetermined portion attributed to regulatory requirements
Construct optimization			
Commercial event selection			
Breeding & wide-area testing			
Regulatory science	Public and private direct costs constructed for single events in single markets	Public and private direct costs assumed or based on exogenous estimates	Private direct costs calculated for global introduction of event
Registration & regulatory affairs			
Opportunity cost	Not included	Indirect costs calculated	Not included
Relative areas in Figure 2	A+B	A+B+C	A+D

To put this into context, Figure 2 shows how these different estimates corelate and overlap. The constructed cost approach generally limits the analysis to areas A+B of Figure 1, while welfare economists are concerned about A+B plus the opporunity costs (C). In contrast, the biotechnology firms are exclusively interested in their cost and benefits, focusing on A+D; while they are concerned about their share of the imputed opportuntiy costs (part of C), they seldom try to make their case based on this type of analysis. This disconnect is somewhat puzzling, as the opportunity costs of delay (C) are have the largest impact on the long-term returns of any new technology. One possible explanation is that while opportuity costs represent real value in the context of new technology development, most of it does not directly accrue to the biotechnology firms themselves, but instead flows to producers and consumers.

Figure 2: The relationship between different estimates of regulatory costs



4.1 CONSTRUCTED COST ANALYSES

More than 65 cost estimates were developed by three groups of economists (which were organized into 10 different teams to calculate different types of estimates for various products and markets): Carl Pray from Rutgers led a series of cost estimates for products in Asia; Nicholas Kalaitzandonakes from University of Missouri/Columbia worked with a team to estimate costs for regulatory compliance for HT and Bt maize/corn in the US, EU, Canada, Argentina, Australia, China, Japan, Korea and the Philippines; and Jose Falck-Zepeda from IFPRI has worked with a range of economists to develop estimates across a range of food and non-food crops in developing countries.

One challenge with much of the general literature is that the explicit methodologies for constructing the cost estimates are often not fully disclosed. In this case, though, the three main teams have offered detailed disclosures of what is included and excluded, and in many instances offer illustrations or details on how the costs were imputed or derived. Table 2 shows the array of explicit costs identified in each of those studies. While the terminology and descriptions vary, for the most part they consistently include most of the same activities generally required for regulatory compliance. All biotech crops are subjected to a battery of tests and significant regulatory scrutiny before commercialization. To identify these general categories of compliance costs, lead scientists and regulatory affairs practitioners (identified through a review of regulatory submissions) were interviewed in Kalaitzandonakes, Alston and Bradford (2007). In addition, data were collected

through assessment of representative dossiers for various novel maize traits submitted over the past 10 years. Using these representative dossiers and the relevant data provided by biotech developers, costs were structured by identifying aggregate categories that were characteristic across all types of dossier submissions. Finally, the authors undertook an evaluation of the degree of overlap among multiple submissions for the same technology across various national regulatory systems and the incremental compliance costs associated with each additional international market where regulatory approval was sought. Pray et al. (2005) report data were also gathered from a number of private companies and from national regulators.

Table 3: Methodologies and categories of costs considered

	Kalaitzandonakes, Alston and Bradford 2007	Pray et al. 2005	Falck-Zepeda et al. 2006
Pre-submission costs	Yes	Yes	Yes
Molecular work	Composition assessment; development of ELISA test; production of tissues	Expression in oils and lint; gene stability	Molecular characterization and testing; ELISA development
Animal safety	Performance and safety studies	Performance and safety studies	Poultry, goat, cow and fish feeding studies
Food safety	Protein testing; 90 day rat toxicology trial	Brown Norway rat allergenicity trial	90 day rat toxicology and allergenicity trials
Environmental safety	Non-target organisms studies; agronomic and phenotypic assessment; environmental fate studies; stewardship	Pollen flow; soil microflora; Greenhouse trials, limited field trials, multi-location field trials, large-scale trials, large-scale farm trials	Gene flow; impact on non-target organisms; agronomic and phenotypic assessment Baseline and follow-up resistance studies; Non-target organism studies
Regulatory fees	Yes	Yes	Yes
Regulator expenses	Yes	Yes	Not clear
In-house costs	Facility and management overhead	Salaries and overhead expenses	Salaries and overhead costs
Socio-Economic studies	Na	Yes	Yes
Post Approval Costs	Na	IPM package	Na

While we have more than 65 cost estimates, we have segmented the constructed cost studies into two categories. We were able to isolate 49 cost estimates developed by the three leading research teams for three key crops (maize/corn, cotton and soybean) and two key technologies (HT and Bt) that had well disclosed methodologies. Each of these products achieved regulatory compliance and commercial entry into at least one market in the period under review. Those studies are presented in Table 4 and are the focus for the meta-analysis that follows.

Table 4: Estimates for regulatory approval costs for cotton, maize and soybeans						
Product	**Trait**	**Crop type**	**Country**	**Approval Cost $US 000**	**Approach**	**Author/Year**
Cotton	Bt	Non food	India	$1,999	Ex post	Pray et al. 2005
	Bt	Non food	China	Private: $89.50 Public: $53.00-$61.00	Ex post	Pray et al. 2006
	Bt	Non food	Indonesia	$93.50	Ex post	Falck-Zepeda et al. 2006
	Ht	Non food	Indonesia	$112.48	Ex ante	
Maize	Bt	Food	China	$500 (private)	Ex ante	Pray et al. 2006
	Bt	Food	Philippines	$1,700	Ex post	Falck-Zepeda et al. 2006
	Bt	Food	India	$500-$1,500	Ex ante	
	Bt	Food	Kenya	$980	Ex ante	
	Ht	Food	Indonesia	$106.85	Ex ante	
	Bt	food	US	$6,790-$14,840	Ex post	Kalaitzandonakes, Alston and Bradford2007
	Ht	Food	US	$5,910-$13,910		
	Bt	Food	EU	$6,870-$14,530		
	Ht	Food	EU	$6,140-$14,315		
	Bt	Food	Argentina	$6,640-$14,575		
	Ht	Food	Argentina	$5,910-$13,910		
	Bt	Food	Canada	$6,680-$14,320		
	Ht	Food	Canada	$5,950-$14,105		
	Bt	Food	Australia	$6,640-$14,515		
	Ht	Food	Australia	$5,910-$13,910		
	Bt	Food	China	$6,640-$14,515		
	Ht	Food	China	$5,910-$13,910		
	Bt	Food	Japan	$6,640-$14,515		
	Ht	Food	Japan	$5,910-$13,910		
	Bt	Food	Korea	$6,64-$14,515		
	Ht	Food	Korea	$5,910-$13,910		
	Bt	Food	Philippines	$6,640-$14,515		
	Ht	Food	Philippines	$5,910-$13,910		
Soybeans	Ht	Food	Brazil	$4,000	Ex ante	Falck-Zepeda et al. 2006

Another 17 studies offered estimates of costs to gain regulatory compliance for a range of other crops, but all were ex ante assessment of products that had not completed regulatory review during the period under review, and in many cases the methodology and data sources were less than complete (Table 5). While these offer a tantalizing glimpse into the dispersion of costs over a wider range of countries, crops and traits, they are qualitatively different than the studies presented in Table 4 and mindful of the directions in Executive Order 12866, we have not formally incorporated these into our meta-analysis.

Table 5: Estimates of regulatory approval costs for other crops						
Product	**Trait**	**Crop type**	**Country**	**Approval Cost $US 000**	**Approach**	**Author/Year**
Rice	Bt	Food	Indonesia	$73	Ex ante	Falck- Zepeda et al.2006
	Bt	Food	India	$1,500 - $2,000	Ex ante	Falck- Zepeda & Cohen 2006
	Bt	Food	Costa Rica	$2,800	Ex ante	Falck -Zepeda & Cohen 2006
	Beta-carotene SGR1	Food	Philippines	$134.5	Ex ante/Ex post	Falck- Zepeda et al.2006
	Xa21 Bac. Blight R.	Food	Philippines	$127.6	Ex ante/ Ex post	Falck-Zepeda et al.2006
Rice	Bt	Food	Philippines	$690.7	Ex ante	Bayer, Norton and Falck-Zepeda 2010
Beans	VR	Food	Brazil	$700	Ex ante	Falck- Zepeda & Cohen 2006
Vegetable	Na	Food	India	$4,000	Ex ante	Falck- Zepeda & Cohen 2006
Potatoes	Bt*	Food	South Africa	$980	Ex ante	Falck- Zepeda & Cohen 2006
	Na	Food	Brazil	$980	Ex ante	Falck- Zepeda & Cohen 2006
Jute	Na	Non Food	India	$1,000 - $1,500	Ex ante	Falck- Zepeda & Cohen 2006
Mustard	Hybrid	Food	India	$4,103 - $5,103	Ex post/ Ex ante	Pray, Bengali and Ramaswami 2005
Eggplant	Bt	Food	India	$53.6	Ex post/ Ex ante	Pray, Bengali and Ramaswami 2005
	Bt	Food	Philippines	$475	Ex ante	Bayer, Norton and Falck-Zepeda. 2010
Tomato	MVR	Food	Philippines	$475	Ex ante	Bayer, Norton and Falck-Zepeda. 2010
Papaya	RSV	Food	Philippines	$248.5	Ex ante	Bayer, Norton and Falck-Zepeda. 2010
	Delayed Ripening	Food	Philippines	$349.2	Ex post	Falck- Zepeda et al.2006

The 49 estimates presented in Table 3 suggest that the average cost of regulatory compliance for a single new trait in a single market is US$7.8 million, with a minimum cost of US$53K and maximum of US$14.8 million (Table 6). For the purposes of this study we are interested in determining whether the costs differ significantly based on four key sets of moderators. First, about half the reviews examined candidate crops with Bt and half with HT traits: given their different agronomic and environmental effects in different markets, that could affect the cost of compliance. Second, not all of the crops were targeted on the food market. Most Bt cotton was not intended for human consumption (even though a small amount of cottonseed oil is

consumed) but most corn and soybeans were assumed to be available for direct human consumption (even though most early innovations were directed to varieties that were predominantly used as animal feed). Third, the nature of the market being contested could conceivably affect the nature of the review: about one third of the estimates looked at reviews by importing countries and the rest by exporting countries. Finally, it is possible that the timing of the evaluation may affect the nature of the estimate: most of the evaluations involved drawing explicit ex post evidence from regulators or proponents on the costs of the process; a few were ex ante constructions based on theoretical assays or expert judgment.

Table 6: Average costs categorized by moderator

	N	Mean	std dev	Min	Max
All studies	49	7,808,272	5,384,964	53,000	14,840,000
Bt trait	28	7,112,000	5,670,146	53,000	14,840,000
HT trait	21	8,736,635	4,825,553	106,850	14,315,000
Food uses	43	8,841,787	4,924,380	106,850	14,840,000
Non-food uses	6	401,413	714,742	53,000	1,999,000
Net exporter	16	8,217,438	5,025,254	500,000	14,840,000
Net importer	33	7,609,889	5,540,118	53,000	14,530,000
Ex ante study	7	1,099,904	1,268,629	106,850	4,000,000
Ex post study	42	8,926,333	4,981,180	53,000	14,840,000

On a first cut, while there is no statistical evidence to suggest that Bt or HT crops are dealt with differently or that exporters and importers impose different regulatory burdens on GM crops, there is some support for the notion that crops intended for use as human food are more costly to regulate than non-food uses (Table 6). Finally the data suggests that ex post studies generate cost estimates on average eight times ex ante projections—which is statistically significant.

One aspect not considered is whether the nationality or corporate status of the developer affects regulatory costs. There is some anecdotal evidence that some developing countries (esp. China, India and Brazil) may impose higher assessment costs on events proposed by multinational corporations (perhaps because they are first-movers or perhaps as an anti-competitive action by governments); in contrast, local public sector institutes producing competitive traits appear to have lower costs and speedier reviews (Pray 2013). At a minimum we know that both the Chinese and Indian governments have programs to subsidize the cost of regulatory approvals for government research institutes and local private companies, but not for private companies (this could affect the constructed costs but would not lower the overall cost of regulation). While it would be worth testing further for this, it is not always clear in the 49 identified studies how the regulators or

subsidy programs judge the provenance of the events considered—quite often candidate GMOs are the product of a collection of partnerships involving public, private and collective actors, making it difficult to clearly assign provenance. As a result, we have not included this as a moderator.

4.2 ECONOMIC WELFARE ANALYSIS

A second approach is to use the direct costs of regulatory compliance to generate a range of indirect costs that result from those outlays. Direct costs include all those items in Table 2, such as research, laboratory and field trials, preparation of dockets, fees and charges paid by proponents and the corresponding expenditures by the regulators to assess and adjudicate the evidence. Indirect costs include the opportunity costs faced by biotechnology companies (as they incur debt servicing charges while revenues are delayed), farmers (who forgo income that could be generated by adopting the new crop) and consumers (who under normal circumstances derive larger consumer surpluses from more productive and lower priced or higher quality products).

A number of economists have attempted to calculate the absolute and relative costs of the regulatory process. Most of the economists conclude that the time it takes to complete regulatory oversight is more important than the actual out-of-pocket direct cash costs. Smyth and Phillips (2002) estimated that if Monsanto and AgrEvo had waited to commercialize their HT canola until they gained regulatory acceptance in Japan, they would have incurred a two-year delay and a major opportunity cost. This ex-post analysis calculated that, by adopting an identity-preserved production and marketing regime to channel the asynchronously approved varieties to the accepting North American market, the companies accelerated adoption by two years, which was estimated to have generated a net present value in 1995$ of more than C$100 million. Pray, Bengali and Ramaswami (2005) also discovered that the two-year delay (pause) in the approval of Bt cotton in India led to aggregate losses to farmers alone of more than US$100 million.

Bayer, Norton and Falck-Zepeda (2010) undertook a sensitivity analysis in their regulatory study to evaluate the effects of increasing regulatory costs and altering the time required for regulatory approval and, hence, adoption of the technologies by farmers. They found the effects on total net benefits of increasing the direct cash costs of regulatory compliance in each case were small, even with four-fold increases. They estimated less than a US$1 million change in NPV in most cases, with the impacts varying from a 1% decrease for rice and papaya traits to a 7% decrease

in the case of MVR tomato. These losses were small compared to the opportunity costs that were incurred when commercialization was delayed from one to three years in the regulatory system. A one-year delay in adoption resulted in a 12% decrease in the projected NPV for Bt rice and up to a 36% decrease for MVR tomato while a 3-year regulatory delay was estimated to cause a 34% drop in the NPV of Bt rice compared to the baseline and a 93% decline for MVR tomato.

There is some supporting evidence that these costs may actually be incurred, as the Phillips McDougall study discussed below reports that firms in 2011 faced a regulatory process that was on average 21 months longer than before 2002. This undoubtedly generates significant opportunity costs to developers and users.

4.3 THE INDUSTRY ESTIMATES

In 2011, Crop Life International, a global federation of the top eight agricultural biotechnology companies and 16 national industry associations, commissioned Phillips McDougall, a consultancy based in England, to survey member companies to determine the cost and duration associated with the discovery, development and authorization of a new biotechnology-derived plant trait that had received cultivation approval in two countries and import approvals from at least five countries. Six multinationals which have undertaken this task were surveyed (i.e. BASF Corporation, Bayer CropScience, Dow AgroSciences, DuPont /Pioneer , Monsanto Company and Syngenta AG); five provided cost estimates for the discovery and construct optimization phases and all offered advice on the costs they incurred downstream , including their regulatory costs. The study reported that the mean cost associated with the discovery, development and authorization of a new biotechnology derived crop trait introduced in the 2008 to 2012 timeframe was US$136M. While the study reported that the costs of meeting regulatory requirements amounted to US$35.1M (only 25.8% of total costs), that may only be part of the story. The evidence presented regarding the mean number of units evaluated at each stage of the development process suggests that firms are now doing more upstream research on discovery opportunities and constructs before they converge on a narrower set of commercial events that they target for introgression, selection and assessment. While the study does not explicitly relate this change in research design to the regulatory costs, it is likely that some of those changes are in response to the evolving regulatory processes.

Table 7: Industry estimates of the discovery, development & authorization costs of a plant biotechnology trait						
Category	Cost $US million	Mean number of units evaluated		Duration of each stage in process (months)		
		For event before 2002	For event 2008-12	For event before 2002	For event 2008-12	To complete in 2011
Total discovery cost	31.0			55.3	53.9	46.3
Early discovery	*17.6*	*1638*	*6204*	*38.0*	*33.9*	*25.4*
Late discovery	*13.4*	*302*	*4005*	*17.3*	*20.0*	*20.9*
Construct optimization	28.3	135	511	18.0	27.0	32.8
Commercial event production & selection	13.6	2853	1302	24.0	30.0	34.0
Introgression breeding & wide-area testing	28.0	4	2	40.0	37.2	42.0
Regulatory science	17.9	2	1	50.5	37.2	47.0
Registration & regulatory affairs	17.2	1	1	44.5	48.8	65.5
Total cost and time for an event	**136.0**			**232.3**	**234.1**	**268.0**

Interestingly, the industry estimates are in the same range as the constructed cost analyses reported in section 4.1. The average cost of the 49 evaluations reported in Table 6 was about US$7.8 million, with exporting countries being about 5% more costly than the average and compliance in importing nations costing about 3% less than the average. If those were scaled up to the Phillips McDougall scale, involving two producing countries and five importers, the total cost would be about US$55 million, which while US$20 million higher than in the industry study is still within one standard deviation of the constructed cost estimates. Moreover, one might expect some economies of scale of undertaking the regulatory science, registration and regulatory affairs in seven markets simultaneously. So at one level, there is some convergence between the scholarly and practitioner views of the direct costs of regulatory compliance.

5. EMPIRICAL ANALYSIS

Given the above analysis, we selected the 49 estimates identified and discussed in section 4.1 that examined the direct costs of regulatory compliance (areas A+B in Figure 2) as the dependent variables and identified four moderators along with the intercept as the appropriate variables to test using regression analysis***. Note, this work is provisional as there is some doubt whether all of the cost estimates are independent assessments. Four groups of authors produced most of the assessments, which suggests that there may be some common assumptions and formulae used by each of the teams that may have created collinearity in the estimates.***

The key moderators that one might anticipate would change the scale and scope of the regulatory cost estimates include the GM trait involved, the intended use of the crop, the market context for the regulatory action and the nature of the analysis undertaken. The 49 cost estimates address one of either herbicide tolerance (HT) or insect resistance (Bt); one might anticipate that the costs of compliance might vary given that Bt crops have tended to raise a host of environmental and pest management questions that HT crops have not; based on reviews to date, both crops have raised similar considerations about human and animal safety. Similarly, the intended use of the novel trait under consideration could change the nature of the review. Cotton is generally used as an industrial input to textiles and clothing (although small amounts of cottonseed oils are consumed in some niche markets). Meanwhile, maize/corn and soybeans are both major components of processed foods and significant animal feeds. Market context could similarly matter. Many of those countries that examined these technologies are major producers and exporters while others are largely importers and consumers. A priori it is not clear whether exporters would undertake more extensive reviews than importers, but there is potential that they might differ. Finally, most meta-analyses try to test to see if the conceptual and practical approach to the studies could influence the divergence of results (e.g. Alston et al. 2000 show that the structure of the lags chosen has a major impact on the estimates of the return on investments in gains to research studies). In our case, we were able to determine whether the cost estimates were constructed before the regulatory process began (e.g. an *ex ante* analysis) or whether they were undertaken after the process had begun or completed. One might expect the two approaches to deliver different results, depending on the prescience of the analysts and the degree of optimism underlying the assumptions about the scale and scope of what would need to be done to satisfy the regulators.

Table 8: Correlation matrix of the instrumental variables

	Total cost	Bt	HT	Non-food	Food	Net exporter	Net importer	Ex ante
Total cost	1							
Bt	-0.19	1						
HT	0.19	-1.00	1					
Non- food	-0.76*	0.20	-0.20	1				
Food	0.76**	-0.20	0.20	-1.00	1			
Net Exporter	0.17	-0.01	0.01	-0.13	0.13	1		
Net Importer	-0.17	0.01	-0.01	0.13	-0.13	-1.00	1	
Ex ante	-0.48	0.00	0.00	0.03	-0.03	0.09	-0.09	1
Ex post	0.48**	0.00	0.00	-0.03	0.03	-0.09	0.09	-1.00
Statistically significant at 95% (*) and 99% (**)								

Table 8 shows the correlation matrix for the dependent variable, regulatory approval costs, and the eight possible moderators. The coefficients of correlation for the trait, use, context or method indicate a variation in the relationship between these independent variables and the cost of approval. Traits do not seem to have a major effect on costs: the HT variable has a low positive correlation with overall cost while Bt crops appear to *ceteris paribus* incur lower regulatory costs; neither is statistically significant in this analysis. The sign and coefficient for non-food use suggests a negative correlation with cost of approval; in other words, the cost of approval is likely to be lower if the trait is intended for a non-food use. The food-use variable shows the obverse effect. Both are statistically significant, suggesting they may be major drivers of the cost structure. The net-exporter variable, which represents those countries producing exportable surpluses of the specific crop under review, shows a small positive correlation that is not statistically significant; the net importer variable is the obverse. Finally, the type of analysis for measuring costs shows some evidence of a relationship. Those studies that used an ex post approach are positively correlated with higher costs; this is statistically significant. Given that the moderators are paired and have perfect negative correlation, we will only use one of each of the pairs (that is Bt/HT, non-food/food, net exporter/net importer and ex ante/ex post). The rest of the correlation matrix shows that the correlation coefficients between independent variables are not significantly different than zero, which provides prima facie support that OLS will generate unbiased and efficient estimates.

We undertook a basic regression where:

$$Ln\,(y_t) = a + b'X + \epsilon,$$

and

Yt is the cost of regulatory approval (put into log linear form),

a is the intercept,

b is the vector of slope coefficients,

X is the matrix of independent variables and

ϵ is the error term.

The regression model consists of four independent variables that are dichotomous dummy variables indicating the presence or absence of a particular characteristic for the key moderators. The specific moderators chosen were HT, non-food use, net exporter and ex-ante analysis. The ordinary least squares model uses the natural log of the dependent variable (the total cash costs of

regulatory compliance in US$ millions), which allows us to test the effect of the explanatory variables in percentage terms instead of units.

As a general rule, regression models include a constant or intercept term (Greene 2002). The constant term explains the variation in the registration costs that are independent of the explanatory variables. For example, a consumption regression model includes a constant term to show that individuals consume regardless of income. In the context of this paper, omitting the intercept term would suggest that variation in registration costs are solely determined by the independent variables under study, which would not likely be realistic. Hence, we have included the intercept, which can be interpreted as the benchmark cost of regulating a new GM trait in a single undifferentiated market. To test this, we removed the intercept to see if it might change the nature of the analysis.

Two models (with and without the intercept) were tested (Table 9). Model 1 results suggest that the independent variables account for approximately 81% of the variation in costs of approval. The coefficient for HT is modestly positive but statistically insignificant, so we are unable to draw any inference of whether the trait has any material effect on costs of regulatory compliance. In other words, the trait of the GM crop has little or no impact on costs of approval *based on the model presented and the data examined*. All of the other variables are statistically significant. The coefficient for non-food use suggests that regulatory costs are lower for GM crops that are not destined for human consumption. The coefficient of -3.68% for non-food is statistically significant at the 10% level of significance, which implies that the intended use for a GM crop (i.e. as a food, feed or industrial application) is a significant factor in the total regulatory approval cost. This intuitively fits with observations from regulators and product proponents—human safety is paramount in regulatory systems. The trade context also has a major impact on costs—exporting countries impose more expensive regulatory processes than importing nations. This is open to a number of different interpretations. One possibility is that exporters are also going to be major producers, so they would need to do both extensive food and feed trials *and* environmental assessments; importers might be able to simply focus on food and feed impacts. A second interpretation is that some of the incremental costs of gaining compliance in net exporting countries may be skewed by the inclusion of the mega-adopters (US, Argentina, China, Brazil, Canada and India) with some countries less enthusiastic about the technology (especially the European Union and some African nations), which subject foreign GM crops to 'less favourable'

conditions (especially delays in decisions, which do not impose extra cash costs) to protect domestic crops from competition from GM exports . A third possibility is that the lower cost of approval in net importing countries may be due to the nature of the specific approvals that have been costed in our dataset. Many developing countries are quite open to GM technology and see it as a way of enhancing food security; in that context, some countries accept foreign data in their regulatory system. Bayer, Norton and Falck-Zepeda (2010) argue that the acceptance of foreign data resulted in lower costs of approval in The Philippines. Finally, the negative sign for the ex-ante assessments suggests that on average those analysts conducting their analysis prior to submission to the regulatory approval body are more optimistic (or less grounded in the nature of the process). The large difference in ex ante and ex post analyses may arise from unexpected multiple trials and requests for evidence that emerge in the approval process which would clearly make the costs 'after' submission much higher than estimates before the GM crop enters the approval process. In essence, optimism appears to dominate and underestimates of the costs are made.

Table 9: Meta-analysis regression results

Default Category	Independent variable	Model 1	Model 2
	Intercept term	15.77	-
Bt	Ht	0.15	11.6
Food	Non Food	-3.68*	7.79
Net importer	Net exporter	0.43*	2.76
Ex post	Ex ante	-2.25**	3.1
	Model R^2	0.81	-0.31
	No. of Observations	49	49

****** Statistical significant at 99%; *Statistically significant at 90%

For completeness, we present model two that tests the hypothesis that trait, product use, trade status and measurement are the only factors impacting costs of regulatory approval. We removed the intercept and found that the overall quality of the regression and the role of specific variables deteriorated—the R^2 dropped and none of the coefficients were significant or had the expected signs in this specification. Therefore, model 1, with the intercept, is preferred empirically.

6. CONCLUSION AND RECOMMENDATION

This article has summarized the state of knowledge about the costs of regulatory compliance for GM crops, adding both conceptual clarity to the diversity of estimates of regulatory costs and new evidence from a meta-analysis. The review of studies done to date shows some

degree of convergence, with the constructed cost estimates higher but still not statistically different than the industry views. The meta-analysis further showed that the context for regulatory reviews—particularly the trait and the market orientation of the respective country—have significant effects on the cost of compliance. Moreover, the nature of the review—whether ex ante or ex post—fundamentally alters the estimates.

One might think that over time we should see greater clarity in the estimates. While that would be helpful, the current estimates are deficient in a few ways. First, there are important indirect costs of staggered approvals, with different traits often being approved at different times in different countries; this is not captured in any of the extant studies. Moreover, none of the studies to date have explicitly examined the costs of gaining approval for stacked traits, which now represent about 25% of global GM area. Regulators presented with stack traits seem to have a practice of not simply assessing the added traits—they also revisit and require full assessment of those previously approved traits that are part of the stack, This likely adds significantly to costs.

In other technology areas, familiarity and experience has tended to lead to convergence of methods and costs of assessing applications. While in a perfect world this might occur, the international conflict over the role of GM technologies in the global food system, combined with the competitive practices of individual firms seeking to develop and introduce new traits, suggests that convergence may be a ways off. This study offers some evidence that the conflict between the mega-adopters and a few key importing and competing markets (especially the EU) has a real and measurable effect on the costs of regulatory compliance and the use-benefits that would be expected to flow to producers, innovators and consumers around the world (other studies, including Haggui, Phillips and Gray 2006 and Paarlberg 2008 offer complementary evidence of this multiplier effect). Meanwhile, there is ample evidence that firms regard their capacity to satisfy regulators as a major competency and competitive advantage, so that they have limited incentive to share their tacit knowledge of the regulatory process and to develop best practices that could lower the barriers to market entry.

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