a compound's true value and region-specific issues. Patients are keen to provide input for clinical trial design, outcome measures, recruitment materials and feedback to participants. Digital patient communities are one such avenue for involvement from those living with chronic illness as these platforms provide rapid, anonymous and convenient methods for hundreds or even thousands of patients to respond to questions over the course of mere days[8]. Successes to date include the rapid development of patient questionnaires and input on challenges inherent in clinical trial protocols. Key success factors include using a wide sample of patients, fostering a reciprocal relationship built on trust, providing feedback and continually assessing the value of incorporating patient views into existing processes[9]. Although high-tech platforms have advantages, such as speed, an in-person 'high-touch' approach may provide more subtle advantages, such as encouraging decision makers to put a face to the patient and think carefully about terminology[10].

However, this approach may require additional time and resources, although time may be saved in avoiding protocol amendments or failed launches. Concerns about tokenism[5] are valid, and researchers should clarify that patients' views will be synthesized with other sources of input. So-called representativeness can sometimes be used as an excuse not to listen to patients but may be overcome by using stratified recruitment or sample weighting to maximize generalizability. Commercial confidentiality can be maintained through tools, such as conjoint analysis, that might ask patients to choose from a range of hypothetical scenarios rather than respond to actual protocols.

Perhaps the biggest challenge, though, is cultural. Patients in 'fellowships' (i.e., a temporary period of employment and mutual learning of an engaged patient embedded within the organization with roles and responsibilities) could maximize the cultural change within a manufacturer, complementing the high-tech approach. Innovative companies should begin experimenting with integrating patient research partners into their decision-making process, building on the successes and failures of other actors in the healthcare system. Ultimately, those who can align their strategy, portfolio and execution with patient value will be the winners.

COMPETING FINANCIAL INTERESTS
The author declares competing financial interests: details are available in the online version of the paper.

Paul Wicks[1], Maria Lowe[1], Susan Gabriel[2], Slaven Sikirica[2], Rahul Sasane[2] & Stephen Arcona[2]

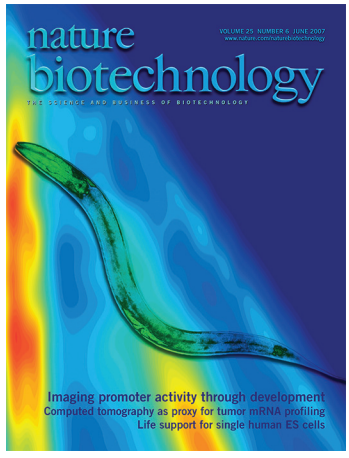
[1]PatientsLikeMe, 155 2nd Street, Cambridge MA, 02141, USA. [2]Novartis, Health Economics & Outcomes Research, One Health Plaza, East Hanover, NJ, 07936, USA.
e-mail: pwicks@patientslikeme.com

1. Hughes, V. *Nat. Biotechnol.* **33**, 14–17 (2015).
2. Hibbard, J.H., Mahoney, E.R., Stock, R. & Tusler, M. *Health Serv. Res.* **42**, 1443–1463 (2007).
3. Mullard, A. *Nat. Rev. Drug Discov.* **12**, 651–652 (2013).
4. Fleurence, R. *et al. Health Aff.* (Millwood) **32**, 393–400 (2013).
5. Arnstein, S.R. *J. Am. Inst. Plann.* **35**, 216–224 (1969).
6. de Wit, M.P.T., Koelewijn-van Loon, M.S., Collins, S., Abma, T.A. & Kirwan, J. *Patient* **6**, 179–187 (2013).
7. Perlmutter, J. *Breast Diseases: A Year Book Quarterly* **22**, 21–24 (2011).
8. Wicks, P. *Trials* **15**, 172 (2014).
9. Garces, J.P.D. *et al. Eliciting Patient Perspective in Patient-Centered Outcomes Research: A Meta Narrative Systematic Review. Mayo Clinic, Rochester. Retrieved January* **20**, 2013 (2012) http://www.pcori.org/assets/Eliciting-Patient-Perspective-in-Patient-Centered-Outcomes-Research-A-Meta-Narrative-Systematic-Review.pdf.
10. Lavallee, D.C., Wicks, P., Alfonso Cristancho, R. & Mullins, C.D. *Expert Rev. Pharmacoecon. Outcomes Res.* **14**, 335–344 (2014).

Conflict of interests and evidence base for GM crops food/feed safety research

To the Editor:

A survey published in your pages several years ago[1] and a more recent review published elsewhere[2] indicate that there are >32,000 papers in the literature relating to genetically modified (GM) crops food and feed. Of those papers, only a subset relate specifically to human and environmental health risks. Although analyses of the literature have consistently concluded that the hazards associated with the use of GM crops are no greater than those for conventionally bred crops[2], naysayers in the public debate continue to raise questions about the safety of these crops, citing a too-limited pool of original studies on GM crops food/feed safety and a surfeit of studies in which outcomes may have been compromised because conflicts of interest (COIs) may have introduced bias and de-emphasized risks[3–5]. Here, I present an assessment of original research papers addressing food/feed safety aspects of GM crops published in peer-reviewed scientific journals (hereafter referred to as reports) with a view to defining the extent of literature related to food/feed safety and examining the issue of COIs.



The survey by Vain[1] published 9 years ago indicated that by 2006, >31,848 reports had been published in the literature relating to GM crops food/feed. However, most of those reports were not original research papers but abstracts, notes, opinions and commentaries not subjected to peer review. Of those reports, only 237 were found to be original research papers and deal specifically with GM crops food/feed safety matters, including detection and compositional, toxicological and nutritional analyses[1]. Last year, Nicolia *et al.*[2] compiled a list of scientific papers on GM crops safety and analyzed them to determine the distribution and composition of literature, covering studies published from 2002 to October 2012. This latter review cited a total of 1,783 reports, including original research papers, reviews, relevant opinions, commentaries and reports addressing all the major issues that emerged in the debate on GM crops. Of those 1,783 papers, 770 were related to GM crops food/feed safety issues.

In the present study, a search of the US National Center for Biotechnology Information's PubMed and Thomson Reuters' Web of Science literature databases using search terms from the studies mentioned above was carried out[1,2] (**Supplementary Table 1**). In addition, I reviewed bibliographical references cited in the

Table 1 Classification of GM food/feed safety research reports according to their main objective of research, and the percentage of each category reporting COIs.

Research area	Number of reports	Percentage without COIs	Percentage that did not declare funding source	Percentage with COIs
Allergenicity potential	46	71.7%	8.7%	19.6%
Animal health	204	67.2%	16.7%	16.2%
Animal nutrition	111	27.9%	18.9%	53.2%
Equivalence	106	43.4%	13.2%	43.4%
Mycotoxins	18	11.1%	22.2%	66.7%
Processing	18	77.8%	11.1%	11.1%
Traceability and/or digestion (DNA or proteins)	91	69.2%	19.8%	11.0%
Unintended effects	104	77.9%	13.5%	8.7%
Total	698	58.3%	15.9%	25.8%

reports to seek additional studies not listed in these databases. The full list of reports identified by the databases and reference analysis is provided in **Supplementary Table 1**. I excluded abstracts, opinions and commentaries from this analysis. To avoid redundancy, I also excluded review articles.

As I was also interested in further understanding competing interests, I decided to analyze our set of papers for financial COIs—those that arise when research is fully or partially funded by a party with a stake in the development of GM crops; and also for professional COIs—those that arise when at least one author is affiliated with a company developing GM crops, even if the research is supported through public funding. To gain insight about COIs, individual reports were manually checked, making it possible to assess information regarding authors' affiliation and funding sources.

A total of 707 original reports were found that met the above criteria. To understand the dynamics of GM food/feed safety scientific publications over a 21-year period (1993–2014), I inspected and considered for further analysis only those 698 reports that had full text access (digital or physical) and a peer-review process before publication. I considered papers regardless of their outcome in terms of potential risks. It is worth noting that fewer than 5% of all reports published reported negative outcomes.

The average number of reports published per year over the past 15 years is 44 (**Fig. 1a**). The continuous and increasing development of new plant transformation events, both private and public (e.g., Hawaii's GM papaya resistant to the papaya ringspot virus developed by scientists from the US Department of Agriculture, DC and Cornell University in New York, and Brazil's GM bean resistant to the bean golden yellow mosaic virus developed by scientists from the EMBRAPA, among others) has led to a continuous characterization and analysis of these newly developed products.

I categorized each of the 698 publications according to the main objective of the study, namely allergenicity potential, animal health, animal nutrition, equivalence, mycotoxins, processing (effects on protein functionality during food manufacturing), traceability and/or digestion (DNA or proteins) and unintended effects (**Table 1**).

The animal health category had the most reports, which included 204 published studies (29.2%). Allergenicity potential had 46 reports (6.6%), whereas mycotoxins and processing had only 18 papers each (2.6%). The remaining categories had ~100 reports each over the period studied.

In terms of COIs, we found that a majority—406 out of 698 reports (58.3%)—have no financial or professional COIs, as the authors were not affiliated with companies that develop GM crops and also declared that the funding sources did not come from those companies. Overall, 180 out of 698 articles (25.8%) had COIs either in terms of the author affiliation or declared funding source. The distribution of COIs across categories is uneven. Over 70% of reports related to three out of the eight categories (allergenicity potential, processing and unintended effect; **Table 1**) show no COIs (financial or professional). Overall, research carried out by scientists unrelated to companies that develop GM crops, but for which the authors did not provide funding information, represented 15.9% of the total reports (111 articles; **Table 1**).

Over half of the reports, 383 (54.9%), were published in journals with a 2012 impact

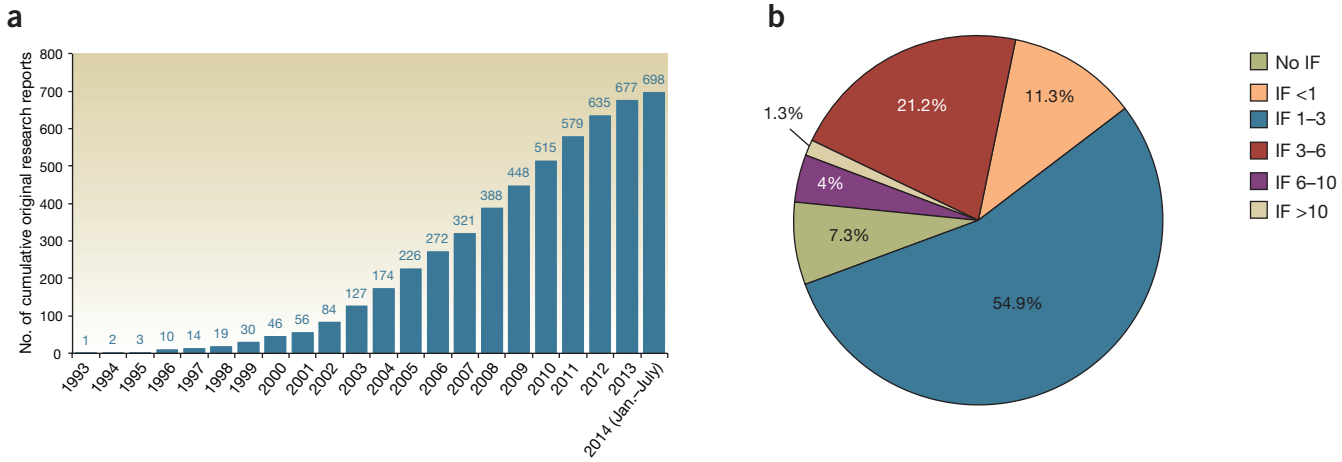


Figure 1 Trends in GM food/feed safety research over the 1993–2014 period. (**a**) Annual production of original research publications focusing on GM food/feed safety (allergenicity potential, animal health, animal nutrition, equivalence, mycotoxins, processing, traceability and/or digestion, and unintended effects). (**b**) Distribution of GM food/feed safety reports according to the 2012 IF of the journals they have been published in (http://wokinfo.com/products_tools/analytical/jcr/). Discontinued journals were assigned their IF at the time of publication.

factor (IF) (http://wokinfo.com/products_tools/analytical/jcr/) ranging from 1 to 3 (**Fig. 1b**). Nine reports (1.3%) were published in journals with an IF higher than ten, whereas 77 reports (11.3%) appeared in journals with an IF <1. Additionally, there were 51 reports (7.3%) published in journals without an IF (**Fig. 1b**). Generally speaking, the IF of journals reporting GM food/feed safety research carried out in agriculture is noticeably lower than IFs of journals associated with high-profile areas of basic or clinical research.

In conclusion, GM food/feed safety issues have been and continue to be extensively studied. The cumulative number of original research reports has dramatically increased over the past years, and publication levels remain high. Different aspects of GM food/feed safety have been addressed from a scientific perspective, and animal health is the most frequently studied topic.

My analysis indicates that only approximately one-quarter of all reports investigated here have COIs related to author affiliation and/or declared funding source, with 15% not reporting funding information. We confirmed that the majority of reports have no conflict from author affiliation and funding source. In other words, at least 58.3% have no COI.

Overall, the analysis of all 698 reports collected here makes it clear that GM crops have been extensively evaluated for potential risks and that genetic modification technologies based on recombinant DNA do not carry a greater risk than other types of genetic modification. Claims either that there is not sufficient peer-reviewed literature evaluating GM food/feed safety issues or that COIs prevail in the published literature are not supported by this analysis.

Note: Any Supplementary Information and Source Data files are available in the online version of the paper.

ACKNOWLEDGMENTS

M.A.S. thanks Drs. H. Campos and W. Parrott for their comments and insights on drafts of this manuscript.

COMPETING FINANCIAL INTERESTS

The author declares competing financial interests: details are available in the online version of the paper.

Miguel A Sanchez

ChileBio, Santiago, Chile.
e-mail: masanchez@chilebio.cl.

1. Vain, P. *Nat. Biotechnol.* **25**, 624–626 (2007).
2. Nicolia, A. *et al. Crit. Rev. Biotechnol.* **34**, 77–88 (2014).
3. Diels, J. *et al. Food Policy* **36**, 197–203 (2011).
4. Robinson, C. *et al. J. Epidemiol. Community Health* **67**, 717–720 (2013).
5. Nielsen, K. *PLoS Biol.* **11**, e1001499 (2013).

Multi-omic data analysis using Galaxy

To the Editor:

Comprehensive multi-omic data acquisition has become a reality, largely driven by the availability of high-throughput sequencing technologies for genomes and transcriptomes[1], and high-resolution mass spectrometry (MS)[2,3] for the in-depth characterization of proteomes and metabolomes. Integrating genomic and proteomic data enables proteogenomic[4] and metaproteomic[5] approaches, whereas integrating metabolomic and transcriptomic or proteomic data links biochemical activity profiles to expressed genes and proteins[6]. Despite the potential for new discoveries, integrated analysis of raw multi-omic data is an often overlooked challenge[7], demanding the use of disparate software programs and requiring computational resources beyond the capacity of most biological research laboratories. For these reasons, multi-omic approaches remain out of reach for many. Here, we describe how Galaxy[8] can be used as one solution to this problem.

A scalable software framework in which disparate omics software could be effectively combined into workflows in an environment accessible to biological researchers would catalyze increased usage of multi-omic approaches. However, there are specific requirements (**Table 1**) for the success of such a framework, making its development far from simple. Although the requirements in **Table 1** are all important, some are crucial for success including the flexibility to accommodate constantly evolving data types and emerging software across omics domains, reproducibility, open and free access, and long-term sustainability.

Fortunately, some frameworks (also known as workflow management systems) already have the potential to meet these requirements. Most prominent among these are the well-established Galaxy[8] and Taverna[9] frameworks. More recently the KNIME (Konstanz Information Miner) platform has been extended for bioinformatics applications[10]; Yabi has emerged as a framework for life sciences computation in high-performance computing environments[11]; the p-GRADE/gUSE framework has been developed for general scientific workflow applications, including biological data[12]; and bioKepler (http://www.biokepler.org/) has been described as an option for large-scale biological data workflow development.

All of these frameworks have been designed with capabilities that meet most of the requirements listed for multi-omic data analysis. Therefore, in principle, one could argue for any of these as an effective choice for multi-omic data analysis workflow development and dissemination. However, in practice, two factors make the Galaxy framework stand out as an excellent, practical choice.

First, Galaxy has been in use for almost a decade and is the most established workflow framework for genomic and transcriptomic data analysis. Numerous reviews on the capabilities of Galaxy have described its flexibility, scalability and amenability to transparent sharing of complete, complex workflows[8]. Importantly, Galaxy contains hundreds of state-of-the-art tools covering two of the core domains (genomics/transcriptomics) that make up multi-omic data analysis applications. For example, numerous Galaxy tools exist for processing and assembling high-throughput sequencing data (e.g., RNA-seq data) and metagenomic data (e.g., whole genome shotgun sequencing or 16S rRNA data), important for proteogenomic and metaproteomic applications, respectively.

Second, Galaxy is poised for wide adoption in the life sciences community. As of June, 2014, some 50,000 users from around the world have registered at the public Galaxy website, and dozens of publicly available local versions of the framework are in use at institutions worldwide (https://wiki.galaxyproject.org/GalaxyProject/Statistics). As of January, 2015 >2,000 publications have cited the use of Galaxy (http://www.citeulike.org/group/16008/). Galaxy is also interoperable with other workflow systems, including Taverna, whose developers have taken steps to make their workflows operable within Galaxy (http://www.taverna.org.uk/documentation/taverna-galaxy/).

Given the practical benefits offered by Galaxy, researchers have recently begun extending the framework for applications beyond genomics and transcriptomics. The move toward multi-omic applications has begun relatively recently. A look at the software tools deposited in the Galaxy Tool Shed under the categories of 'Proteomics' and 'Metabolomics' indicates activity in these