

Article

A Pharmaceutical Bioethics Consultation Service: Six-Year Descriptive Characteristics and Results of a Feedback Survey

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Background: Bioethics consultations are conducted in varied settings, including hospitals, universities, and other research institutions, but there is sparse information about bioethics consultations conducted in corporate settings such as pharmaceutical companies. The purpose of this article is to describe a bioethics consultation service at a pharmaceutical company, to report characteristics of consultations completed by the service over a 6-year period, and to share results of a consultation feedback survey. **Methods:** Data on the descriptive characteristics of bioethics consultations were collected from 2008 to 2013 and analyzed in Excel 2007. Categorical data were analyzed via the pivot table function, and time-based variables were analyzed via formulas. The feedback survey was administered to consultation requesters from 2009 to 2012 and also analyzed in Excel 2007. **Results:** Over the 6-year period, 189 bioethics consultations were conducted. The number of consultations increased from five per year in 2008 to approximately one per week in 2013. During this time, the format of the consultation service was changed from a committee-only approach to a tiered approach (tailored to the needs of the case). The five most frequent topics were informed consent, early termination of a clinical trial, benefits and risks, human biological samples, and patient rights. The feedback survey results suggest the consultation service is well regarded overall and viewed as approachable, helpful, and responsive. **Conclusions:** Pharmaceutical bioethics consultation is a unique category of bioethics consultation that primarily focuses on pharmaceutical research and development but also touches on aspects of clinical ethics, business ethics, and organizational ethics. Results indicate there is a demand for a tiered bioethics consultation service within this pharmaceutical company and that advice was valued. This company's experience indicates that a bioethics consultation service raises awareness about bioethics, empowers employees to raise bioethical concerns, and helps them reason through challenging issues.

Keywords: research ethics, ethics consultation, pharmaceutical bioethics, descriptive research, survey research

Bioethics consultation is an activity that varies in scope depending on the setting. For example, in a hospital or other health care setting, bioethics consultation is understood to be a clinical (or medical) ethics consultation addressing clinical care questions (e.g., surrogate decision making, end-of-life care decisions). In a university setting, bioethics consultation usually is a research ethics consultation, including review of human or animal study proposals and answering

questions about ethical study design and conduct. In some biotechnology settings, bioethics consultation can be similar to that of a university setting but limited to certain topics, such as collection and storage of human biological samples or the ethics of stem cell research. In a pharmaceutical research and development (R&D) setting, many of these mentioned activities are combined, along with some additional aspects unique to a corporate environment.

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Numerous reports of clinical consultation services exist, but reports of research ethics consultation services are limited. These include reports by the Johns Hopkins School of Public Health (Taylor and Kass 2009) and the National Institutes of Health (NIH) Clinical Center (Danis et al. 2012). Closely related are the research ethics consultation services (RECS) developed by institutions receiving Clinical and Translational Science Awards (CTSA) from the NIH. The aim of these RECS is to help researchers and ethicists partner to solve ethical dilemmas and safeguard the protection of human subjects (de Melo-Martin, Palmer, and Fins 2007; Resnik 2008). It was recently reported that RECS exist at 33 CTSA institutions, although usage appears to be somewhat limited, with the majority of RECS surveyed reporting 4 or fewer consultations in the prior year (McCormick et al. 2013). Detailed information on 23 consultations received by a RECS at Stanford University was reported by Cho et al. (2008). Aside from a survey of bioethics consultation practices in Canada (Greenberg et al. 2014), there is little information regarding research ethics consultation services outside the United States.

At Eli Lilly and Company (“Lilly”), a midsize global pharmaceutical company, what we refer to as *pharmaceutical bioethics consultation* focuses primarily, but not entirely, on R&D. Consultations address a broad range of issues, spanning the entire process of drug discovery and development (basic research to Phase 1–4 clinical trials), to medical affairs activities related to the anticipated clinical use of approved drugs or devices. Occasionally, bioethics questions may originate from areas of the company less closely related to drug development, such as public policy or investor relations. As such, the scope and variety of questions can touch on aspects of business and organizational ethics, in addition to bioethics. An example of the type of consultation questions we receive is represented by the following hypothetical scenario:

A study team is planning a clinical trial of a marketed antidepressant in children aged 7–11. The medicine is approved for major depressive disorder in adults in many countries but there are no pediatric data. In the planned trial, children with depressive symptoms will be randomly assigned to one of two 10-week treatment groups, one receiving the company’s antidepressant and the other receiving placebo.

Study sites have been identified in the United States and France, but the anticipated enrollment rate is slow. In order to meet regulatory milestones, the team is considering adding study sites in Indonesia, which is considered an “emerging market” country (typically less developed regarding economic output, health care expenditures, and health status).

In Indonesia, there are several antidepressants on the market but none considered equivalent to the drug under study.

This scenario raises multiple ethical issues, including the use of placebo, prospect of direct benefit for pediatric participants, and post-trial access to the study medicine and other benefits of the research. Because of the interplay

among fields of applied ethics, as well as the multiple stakeholders in a corporate environment, even a seemingly straightforward consultation question can become complex, as demonstrated by this example. Therefore, providing useful advice requires specialized understanding of pharmaceutical R&D, applied ethics, and stakeholder needs, as well as an appreciation of how advice could be utilized by different business areas of the company.

To our knowledge, this article is the first description of a bioethics consultation service within a pharmaceutical company. The purpose of this article is to describe the service; report descriptive characteristics of consultations completed between 2008–2013, including 4-year results of a consultation feedback survey; and promote shared learning from our findings.

BACKGROUND

Organization and Resourcing of Bioethics Program

The purpose of the bioethics program is to assist employees in identifying and addressing bioethics issues and to engage with internal and external stakeholders on bioethics matters related to the pharmaceutical industry. It functions in an advisory capacity and develops and provides resources to achieve its purpose. It addresses company-specific issues in the form of position papers and case-specific issues in the form of consultations.

The bioethics program comprises both full-time and extracurricular (i.e., Bioethics Advisory Committee [“Committee”] members who serve in addition to their full-time jobs) efforts. Full-time staff have specialized education and/or training in bioethics and pharmaceutical industry experience. The Committee consists of senior leaders representing a cross-section of skills relevant to research and development (including physicians, bioethics, clinical operations, discovery research, medical affairs, drug safety, regulatory affairs, veterinary medicine, quality, legal, and public policy), plus two academic bioethics consultants external to the company. All Committee members take research ethics training (CITI Program 2014), and some have additional bioethics training or experience (e.g., institutional review board [IRB] member/chairperson).

Organizationally, the bioethics program is an independent unit, reporting through the chief medical officer and separate from the discovery research and product development organizations. The bioethics program is distinct from the company’s compliance division, which creates and enforces the company’s internal policies (including the employee code of conduct) and carries out investigations of potential violations of policies, regulations, and law.

History of Bioethics Consultation at Lilly

The Committee has conducted bioethics consultations since its inception in 1999, but prior to 2008, only brief qualitative records (i.e., meeting minutes) were kept. In

2008, the first full-time bioethics staff position was created, and from that time, consultations were managed more systematically, including collection of prespecified data on the descriptive characteristics of consultations and program performance (e.g., number of consultations completed, response time). Starting in 2009, the availability of the consultation service was communicated more broadly within the company and a tiered system was instituted to manage workload and improve efficiency.

Bioethics Consultation Process

Consistent with the purpose of the bioethics program, the bioethics consultation service is advisory in nature. Because of this philosophy, there is no systematic monitoring of after-consult action, except for the survey described later.

Consultation confidentiality is respected to foster an environment of trust that encourages exploration of questions without fear of repercussions. Access to the consultation database is limited to bioethics staff, Committee members, and individuals participating in bioethics training. In the event a compliance issue (i.e., any violation of law, regulation, or company policy) is identified during the course of a consultation, confidentiality is overridden by the obligation to report the issue through required channels.

The flowchart in Figure 1 depicts the company’s bioethics consultation process. Bioethics staff members are responsible for contacting the requester, obtaining initial information, and triaging the case to a consultation tier.

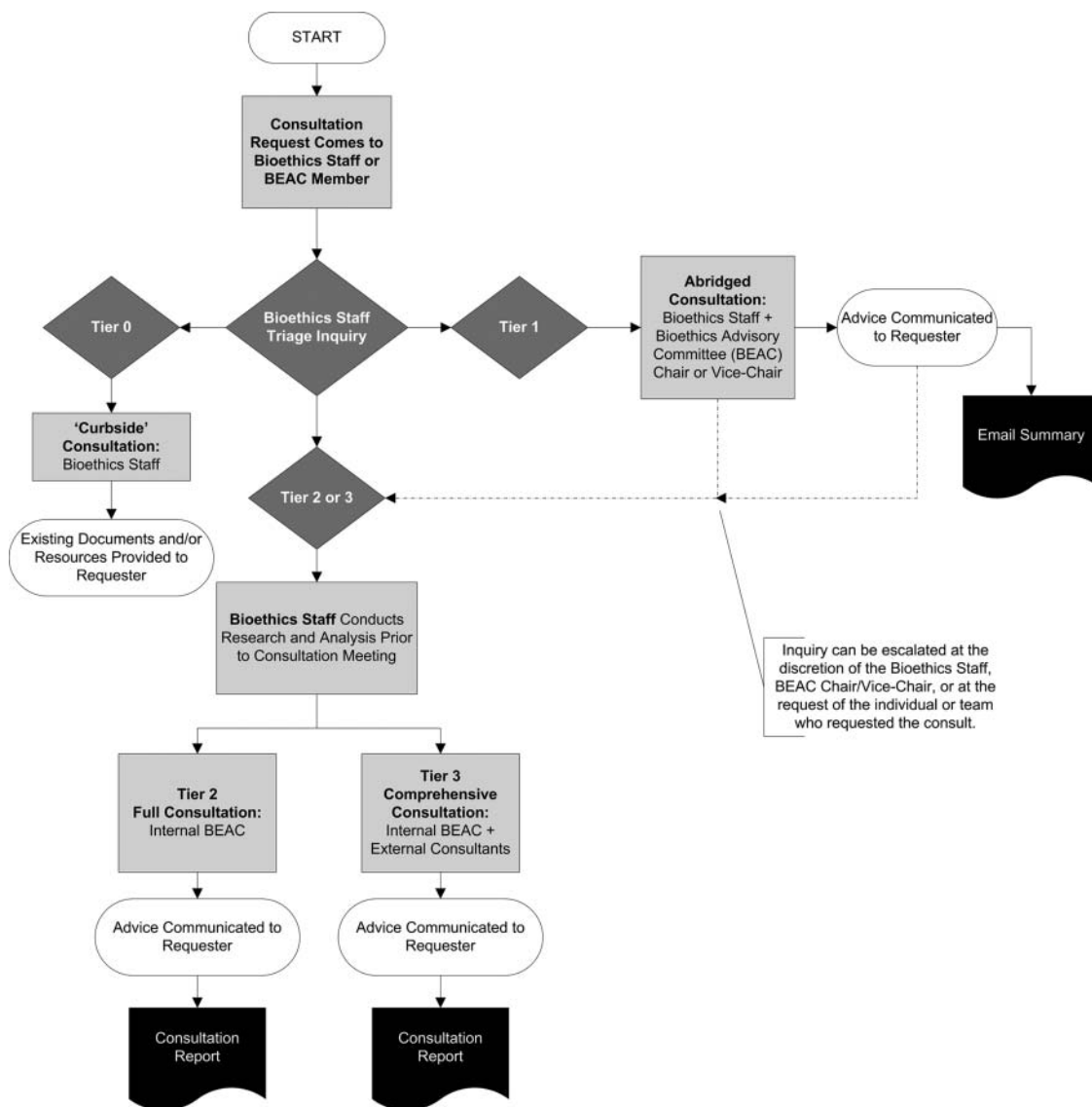


Figure 1. Pharmaceutical bioethics consultation process flow. BEAC = Bioethics Advisory Committee.

The tiered system was adapted from a similar one described on another pharmaceutical company's public website (F. Hoffmann-La Roche Ltd 2003). Tier 0 ("curbside") consultations are relatively straightforward inquiries for which existing documents or other available resources are sufficient to answer the question. This tier of consultation can be addressed by an individual member of the bioethics staff or Committee. Tier 1 (abridged) consultations involve questions not fully addressed by existing resources, but not so complex or broad in scope or impact that they require the input of the full Committee. Bioethics staff members work with the chair or vice-chair of the Committee to formulate a response. Tier 2 (full) consultations are judged to have broad scope and/or impact and require the input of cross-functional leadership or specific expertise. The bioethics staff and relevant internal members of the Committee meet with the requester(s) to discuss the consultation and formulate a response. Tier 3 (comprehensive) designation is reserved for questions that are particularly complex, require external perspective, and/or have a global or broad business impact. In this case, the full Committee (including external consultants) meets with the requester(s). Prior to 2009, all consultations were equivalent to Tiers 2 and 3.

The response-time goal is to acknowledge a consultation request within two business days. Depending on the complexity of the consultation, time to provide advice can vary from a same-day response (for Tier 0 requests) up to weeks or even months for particularly complex consultations (Tier 3) that require research and external perspective. Occasionally, a highly complex case may warrant ongoing consultation, and advice may be provided on the same issue (or variants of the issue) on an iterative basis.

Approach

Consultation advice is developed by referring to the company's bioethics positions on specific issues (<http://www.lilly.com/research-development/approach/research-ethics/Pages/bioethics.aspx>) and the company's bioethics framework (Van Campen, Klopfenstein, and Therasse 2012). The framework is based on bioethics principles (Beauchamp and Childress 2009); a synthesis of ethics guidance documents (e.g., Council for International Organizations of Medical Sciences [CIOMS] 2002; International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use [ICH] 1996; National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research 1978; World Medical Association 2008); and scholarly literature. Our approach to consultations is principles based (i.e., bioethics principles and principles derived from the company's mission, vision, and values), with a view toward maximizing the good of relevant stakeholders.

Bioethics Consultation Summaries and Reports

The format for conveying advice varies with the tier of the consultation. Tier 0 requesters typically receive an email with links to bioethics resources. Tier 1 requesters generally receive a brief email summary of the advice, but may receive a formal report, depending on the requester's needs. Tier 2 and 3 requesters receive a formal report to document and communicate the consultation advice.

The consultation report format was adapted from a clinical bioethics consultation method (Orr and Shelton 2009) and consists of five sections: (1) question, (2) background, (3) assessment, (4) analysis, and (5) recommendations. The question states the question or problem as received from the requester. The background section is a summary of information pertinent to the question. The assessment section is an interpretation of the ethical issue(s) or problem(s) presented by the requester's question. The analysis section evaluates the ethical issues involved, the decision(s) that need to be made, and any available options for resolving the issues. Finally, the recommendations state the bioethics advice derived from the analysis.

METHODS

Data Collection

The consultation database is a Web-based list programmed in SharePoint 2010 (Microsoft, Redmond, WA) and stored in a restricted-permission area on an internal company website. Information pertaining to consultations is entered into the database by bioethics staff (see Table 1 for time-based and descriptive variables analyzed).

The 20 primary topic categories were first devised in 2012. From 2008 to 2012, consultation topics were entered into the database but not selected from a prespecified list, which resulted in more than 80 different topic categories. Because of a need for meaningful reporting on consultation topics, the existing topics were reviewed, redundancies were eliminated, and closely related topics were combined. The resulting list of 20 primary topic categories is shown in Table 2. All historical consultations in the database were reviewed and each was retrospectively assigned to one of these 20 primary topic categories.

The anonymous survey was initiated as a process and quality improvement mechanism, and as a means to assess whether advice was implemented. Four-year survey data were collected on consults completed from the first quarter of 2009 through the fourth quarter of 2012. Quarterly e-mail surveys were sent to requesters immediately following the close of the quarter in which the consultation was completed. The survey consisted of 34 items (see online supplement) with a variety of response formats, including multiple choice, yes/no, free text, and Likert statements. Agreement with the Likert statements was measured on a 5-point scale with verbal anchors of *1-disagree*, *3-somewhat agree*, and *5-agree*. Results were aggregated into an Excel

Table 1. Characteristics of pharmaceutical bioethics consultations by year

	2008	2009	2010	2011	2012	2013
Number of consultations	5	17	12	46	58	51
Mean (range) days to respond	1.8 (0-3)	2.2 (0-22)	0.7 (0-4)	1.2 (0-7)	0.9 (0-10)	1.3 (0-16)
Mean (range) days to provide advice	35.3 (3-122)	23.1 (0-72)	10.4 (0-32)	6.8 (0-64)	4.8 (0-24)	7.1 (0-63)
Most frequent primary topic	(tie) Human Biological Samples and Patient Rights	Informed Consent	(tie) Benefits and Risks and Informed Consent	(tie) Stopping a Clinical Trial and Pediatrics	Informed Consent	Informed Consent
Most frequent phase of development	Preclinical	Phase 3	Phase 3	Non-specific*	Phase 3	Phase 3
Percentage compound- or product-related	0%	76%	67%	78%	81%	80%
Percentage from outside US	0%	6%	0%	8%	13%	8%
Percentage whether/how/both [†]	40%/60%/0%	71%/24%/6%	58%/25%/17%	59%/13%/28%	50%/19%/31%	51%/18%/31%
Percentage of Tier 0/1/2/3 [‡]	0%/60%/20%/20%	0%/76%/0%/24%	33%/33%/33%/0%	41%/39%/13%/7%	40%/52%/5%/3%	45%/41%/12%/2%

* "Non-specific" means that the consultation was not relevant to a specific phase of drug development.

[†] "whether" refers to consultations inquiring *whether* an activity is ethically appropriate. "how" refers to consultations inquiring *how* to conduct an activity in an ethical manner. "% both" refers to consultations that contain both "whether" and "how" elements (Farsides 2003). Percentages may not total to 100% due to rounding.

[‡] Tier 0 = "curbside", Tier 1 = abridged, Tier 2 = full, Tier 3 = comprehensive. Tier 0 was first used as a consultation response level in 2009, and the first Tier 0 consultation was conducted in 2010. Percentages may not total to 100% due to rounding.

Table 2. Frequency of pharmaceutical bioethics consultation primary topics (2008–2013)

Consultation Primary Topic	Number of Consultations (N = 189)	Percentage of Consultations
Informed Consent	30	15.9%
Early Termination of a Clinical Trial	19	10.1%
Benefits and Risks	18	9.5%
Human Biological Samples [†]	17	9.0%
Patient Rights	15	7.9%
Vulnerable Population (Pediatric) [†]	13	6.9%
Compassionate Use ^{*†}	11	5.8%
Continued Access/Post-Trial Access [†]	9	4.8%
Clinical Use of Drug/Device/Diagnostic [*]	8	4.2%
Study Design (Including Use of Placebo [†] and Use of Active Control [†])	8	4.2%
Conduct of Clinical Trial	7	3.7%
Scientific Disclosure/Publication	7	3.7%
Investigative Country/Site Selection ^{*†}	7	3.7%
Internal Company Processes [*]	5	2.6%
Independent Ethics Review	5	2.6%
Vulnerable Population (Non-Pediatric)	4	2.1%
Conflict of Interest	2	1.1%
Incentives for Participants	2	1.1%
External Standards and Guidelines [*]	1	0.5%
Tailored Therapeutics [*]	1	0.5%

* Topics specific to a pharmaceutical R&D or corporate environment, or not seen on topic lists for other closely related consultation services.

[†] Lilly has public bioethics position statements on these topics available at: <http://www.lilly.com/research-development/approach/research-ethics/Pages/bioethics.aspx>

2007 (Microsoft, Redmond, WA) spreadsheet for the relevant quarter.

There was no IRB review of the current research. Lilly does not have an internal IRB, but we believe that this research would be judged as exempt from IRB review. We believe the consultation database analysis is exempt because it does not qualify as human subjects research. Rather, the unit of analysis is the consultation question and the identity of the requester (who may or may not have been the individual who raised the question) is not relevant. The feedback survey analysis could qualify as human subjects research but would be exempt under 45 CFR 46.101(b)(2) as it involved the use of survey procedures and the data were collected anonymously (with no readily accessible means to determine the identity of any one responder). Because the company has a strict policy of nonretaliation for reporting ethics concerns, reporting the survey results presents no obvious risk to the consultation requesters of criminal or civil liability or of damage to their financial standing, employability, or reputation. This policy is widely communicated internally and is posted on the company's public website (<http://www.lilly.com/SiteCollectionDocuments/pdf/RedBook>). As an additional means to respect confidentiality, the consultation information presented in this article is limited to general

topics and reported in aggregate; details on the specific questions, advice, and recommendations are not reported.

STATISTICAL ANALYSIS

The consultation database records from January 2008 through December 2013 were exported into an Excel 2007 spreadsheet. Categorical variables were analyzed via the pivot table function, which provided frequency counts and percentages for each category. Time-based variables (e.g., time to response) were analyzed by creating a new column with the difference between two date variables (in calendar days) and then obtaining the mean for each year and for all six years. If a consultation record had a missing value for a variable, that record was excluded from the analysis for that variable only.

For the consultation feedback survey, requester response spreadsheets from all years were aggregated into a single spreadsheet. Categorical variables were analyzed with the pivot table function as above, and responses to Likert-scale items were averaged for all responders. If a responder had a missing value for a Likert-scale item, that responder's data were excluded from the analysis for that item only.

RESULTS

Characteristics of Consultations

During the 6-year reporting period, 189 consultations were completed. The rate of requests increased approximately 10-fold from 2008 to 2013. Table 2 presents the numbers and percentages of consultations within each primary topic. Although each consultation was categorized under one primary topic, most had up to two additional topics, reflecting the complexity of most cases, as illustrated by the example in the Introduction. Specifically, 13 consultations were recorded under only one topic, 76 had 2 topics, and 100 had 3 topics.

Table 1 presents descriptive characteristics of the consultations by year. The overwhelming majority of consultations (90%) were requested by United States-based employees. The three most common non-United States countries of origin were the United Kingdom, Germany, and Spain.

The majority of consultations (77%) related to a product (i.e., drug, device, or diagnostic) as opposed to a general bioethics issue (e.g., human biological samples). Of the 145 product-specific questions, the most common phase of development at the time of consultation was Phase 3. Total numbers and percentages for each product development phase category across all 6 years were: preclinical: $n = 16$ (8%); Phase 1: $n = 13$ (7%); Phase 2: $n = 20$ (11%); Phase 3: $n = 72$ (38%); and Phase 4: $n = 16$ (8%).

These data also revealed a decrease in the percentage of Tier 3 consultations over time. Total numbers and percentages of consultations for each tier across all six years were: Tier 0: $n = 69$ (37%); Tier 1: $n = 89$ (47%), Tier 2: $n = 20$ (11%), and Tier 3: $n = 11$ (6%).

Consultation Feedback Survey Responses

Of 129 surveys administered, 40 were completed and returned, yielding a response rate of 31% during the 4-year reporting period.

The feedback survey items and responses can be found in their entirety in an online supplement. Highlights of the feedback survey appear in Table 3. In the majority of cases, advice was fully or partially implemented. Free-text comments revealed that often, there were circumstantial reasons that advice could not be fully implemented. Favorable comments were made about the speed of response, thoroughness of the review, and practical nature of the recommendations. Few unfavorable comments were received, but did include the following: One recommendation was viewed as impractical, and communication about the consultation service was viewed as inadequate.

DISCUSSION

To our knowledge, this is the first report describing bioethics consultation in a corporate pharmaceutical environment. The feedback survey results indicate that the

Lilly bioethics consultation service is viewed as approachable, helpful, and responsive, and that advice generally is being implemented. The consultation database results indicate institutional demand for this service has increased over the 6-year reporting period. The rate of consultation requests has increased from 5 per year in 2008 to approximately 1 per week in 2012 and 2013. Although not included in the statistical analysis, consultation rates prior to 2008 ranged from 0 to 5 per year (1999–2007).

Increased utilization of the consultation service is likely due to several changes made in 2009. First, the initiation of proactive communication about the service has increased general awareness. Second, institution of the tiered consultation system has made the service more approachable. The increasing number of consultations is consistent with Loma Linda University Medical Center's experience as it transitioned from a default committee approach for every hospital ethics consultation request to an individual ethics consultant model (Orr 2009). The presumption is that people are more likely to request a consultation if they feel comfortable with the process. A default committee model can be intimidating—much like a “court proceeding,” as Orr observes. If, however, requesters feel confident they can ask a question in a safe (i.e., confidential), nonthreatening (i.e., advisory rather than judgmental) environment, then it is understandable that the rate of consultations would increase.

Third, the initiation of bioethics consultation summaries and reports has made the consultation experience more user-friendly. The summaries and reports are designed to be educational in nature, which requesters find beneficial. A report demonstrates that the Committee took the request seriously and invested significant thought to reason through the requester's issue, and also helps the requester convey the Committee's advice back to colleagues.

Although there was an initial increase in consultation requests, data from the last two years indicate the rate may be leveling off. This apparent plateauing could reflect broader awareness and use of existing resources as the program communicates the existence of the company bioethics framework and continues to develop a library of bioethics position papers on various topics.

The tiered consultation model has also improved efficiency, reducing time to provide advice from 35 days in 2008 to 7 days in 2013. Organizing a meeting of the entire Committee (including external experts) is logistically challenging, therefore prolonging time to provide advice. Advice time can be reduced when using individual consultants (Tier 0) or a subset of the Committee (Tier 1 or 2). The tiered approach also uses internal and external resources more wisely by enlisting additional expertise only when necessary.

The general decrease in advice time and the decrease in the percentage of Tier 2 and 3 consultations over the 6-year reporting period suggest the consultation service is gaining efficiency and skill. As more consultations are completed, individual staff and Committee members have

Table 3. Selected feedback survey items and summarized data from all responders (N = 40)

Item	Possible Responses	n (%) N = 40	M (SD)			
General						
Did you or your team implement the recommendations provided?	Partially	9 (23%)	—			
	Completely	29 (73%)	—			
	Not At All	0 (0%)	—			
	No answer	2 (5%)	—			
Consultation Report						
Please rank the following statements accordingly:						
	1 Disagree	2	3 Somewhat Agree	4	5 Agree	
The report was useful for formulating a plan of action to discuss with business partners or external collaborators or institutions.	1	2	3	4	5	— 4.5 (0.71)
The report was useful internally for discussions with team members or collaborative colleagues.	1	2	3	4	5	— 4.3 (0.87)
Consultation Advice						
The advice helped me (or my team) be more efficient with our decisions (e.g., planning, execution).	1	2	3	4	5	— 4.3 (0.71)
The advice resolved the dilemma that I (or my team) were facing.	1	2	3	4	5	— 4.2 (0.95)
The advice adequately addressed the scope of the issue(s).	1	2	3	4	5	— 4.5 (0.82)
The advice was idealistic or complicated.	1	2	3	4	5	— 1.8* (1.13)
The advice was practical and easy to implement.	1	2	3	4	5	— 4.6 (0.60)

N = total number of responders; n = number of requesters with that response; M = mean, SD = standard deviation.

*Item phrased in reverse direction.

become more experienced bioethics consultants, and the consultation database can serve as a knowledge base to which staff and Committee members can refer. In addition, there is now an internal library of resources to guide consultation advice.

Consultation topics generally were consistent with those in previous reports of research ethics consultations. Our topic list appears to have in common up to seven topics with Johns Hopkins University (Taylor and Kass 2009), four topics with Stanford University (Cho et al. 2008), and eight topics with the NIH (Danis et al. 2012). More specifically, our consultations were generally similar to those reported by Johns Hopkins and Stanford, except for IRB-related questions, and to the NIH, except for clinical (or medical) ethics consultations. Many of our consultation topics could apply to research ethics consultations in any setting (e.g., “informed consent,” “conflict of interest”), but some are more specific to a

pharmaceutical drug development or corporate environment (see Table 2 note). In addition to topics that are more specific to pharmaceutical R&D, it is the convergence of clinical ethics, business ethics, and organizational ethics that distinguishes pharmaceutical bioethics consultation from traditional research ethics consultation.

The most frequent consultation topics we encountered presumably reflect the foremost concerns of employees as they design and conduct clinical trials. Informed consent consistently has been a top consultation topic. This could reflect the high priority employees and regulators place on this important protection for human research participants, but may also point to gaps in existing guidance on informed consent. Another common consultation topic was stopping a clinical trial prior to its planned termination date. When this business action is being considered, employees seek advice to ensure that the welfare of currently enrolled participants is addressed, that the sacrifices and contributions

already made by participants are respected, and that any generalizable knowledge is shared appropriately.

Limitations of the Analysis

One limitation of the consultation database analysis is that most of our consultations addressed multiple topics (e.g., a question about stem cell research was categorized under the primary topic of “Human Biological Samples” but also under secondary topics of “Informed Consent” and “Patient Rights”), so restricting this analysis to only one primary topic per consultation resulted in some loss of information regarding the complexity of the consultations. In addition, primary topic categories were designated solely by agreement between two of the coauthors (LEV and SBW). An independent rater might not have agreed with the methodology. A third limitation was absence of the Tier 0 designation prior to 2010, which resulted in underreporting of Tier 0-like consultations in the earlier years and may partly explain the decrease in Tier 3 consultations over time.

A limitation of the feedback survey analysis was that less than one-third of requesters completed the survey, although this response rate is typical for survey research conducted by e-mail (Sheehan 2001). Still, results may not be representative of all those who requested bioethics consultations. We also acknowledge the limitations of user satisfaction as an outcome measure, as it is only one aspect of program effectiveness.

Finally, all data were collected and analyzed by employees and/or shareholders of Lilly, so freedom from analysis bias cannot be guaranteed.

Limitations of the Consultation Service

A significant limitation of the service is measuring the impact of our advice. The survey is one method, but surveys are limited by response rate and selection bias. It is challenging to find methodology that will adequately measure both positive impact (that which was a desired outcome and did occur) and preventive impact (that which was not a desired outcome and did not occur). Future research might focus on developing reliable measures of improvement in ethical decision making at the organizational level.

Although some could argue that an advisory rather than governance structure is a limitation for a consultation service, we have found it to have certain advantages. First, teams approach the service because they are facing difficult ethical issues and are looking for answers. Because of this, the majority of requesters are very appreciative of the guidance. Second, because teams are not bound to follow the advice, tensions are generally mitigated and the consultation process is interactive and collegial. If a consultation does become adversarial, our action has been to escalate the issue to more senior leadership for resolution.

Some may also argue it is impossible to eliminate institutional bias with a consultation service provided by

corporate employees and paid consultants. We affirm this risk; however, we have structured the service to foster objectivity by organizational independence from product development teams. Independence from development teams is essential because recommendations can result in unplanned work that may cause delays and/or increased cost. If a member of the consultation service is involved with the development project, then that member is asked to recuse him-/herself from the case. Use of external consultants and a consistent bioethics framework also helps ensure alignment with consensus ethical principles established external to the company.

CONCLUSION

Pharmaceutical bioethics consultation is a unique category of bioethics consultation that primarily focuses on pharmaceutical R&D but touches on aspects of clinical ethics, business ethics, and organizational ethics. The demand for pharmaceutical bioethics consultations at Lilly suggests there could be a similar need in other biopharmaceutical companies. Although it is reasonable to expect pharmaceutical employees to identify ethical problems and resolve simple cases, it is probably not reasonable to expect them to reason through more complex cases when doing so is not their primary job. Due to the complexity of bioethics questions in a pharmaceutical environment, the need to consider multiple stakeholders, and the need to provide relevant and actionable advice, it appears necessary to have dedicated, qualified staff, trained committee members, and external experts who can perform the requisite in-depth ethical analysis.

This company's experience indicates that a bioethics consultation service raises awareness about bioethics, encourages employees to raise bioethical concerns, and helps them reason through challenging issues. We consider it to be an important component of fostering an organizational culture of bioethics. This information about our methodology and the scope and complexity of pharmaceutical bioethics consultations is shared in the hope that it may benefit similar institutions and initiate an industry-wide dialogue about what constitutes high-quality pharmaceutical bioethics consultation. ■

SUPPLEMENTAL DATA

Supplementary material for this article can be accessed on the publisher's website.

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AUTHOR CONTRIBUTIONS

The following reflects the contributions of the listed authors: study conception and design: Van Campen, Allen, Watson, and Therasse; data collection: Van Campen, Allen, Watson, and Therasse; data analysis: Watson; initial drafting of article: Watson; review and critical revision of article: Van Campen, Allen, and Therasse.

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CONFLICT OF INTERESTS

All coauthors except Therasse are employees and shareholders of Eli Lilly and Company. Therasse is a retiree and shareholder of Eli Lilly and Company.

ETHICAL APPROVAL

This study was not reviewed by an institutional review board (IRB) because it does not qualify as human subjects research. The anonymous survey procedures used to obtain feedback on the consultation service are typically exempt from IRB review.

REFERENCES

- Beauchamp, T. L., and J. F. Childress. 2009. *Principles of biomedical ethics* (6th ed.). New York, NY: Oxford University Press.
- Cho, M. K., S. L. Tobin, H. T. Greely, J. McCormick, A. Boyce, and D. Magnus. 2008. Research ethics consultation: The Stanford experience. *IRB: Ethics and Human Research* 30(6): 1–6.
- Council for International Organizations of Medical Sciences. 2002. International ethical guidelines for biomedical research involving human subjects. Available at: <http://www.cioms.ch> (accessed January 18, 2012).
- CITI Program. 2014. Collaborative Institutional Training Initiative (CITI) at the University of Miami. Available at: <http://www.citiprogram.org> (accessed February 19, 2014).
- Danis, M., E. Largent, D. Wendler, et al. 2012. *Research ethics consultation: A casebook*. New York, NY: Oxford University Press.
- de Melo-Martin, I., L. I. Palmer, and J. J. Fins. 2007. Viewpoint: Developing a research ethics consultation service to foster responsive and responsible clinical research. *Academic Medicine* 82(9): 900–904.

F. Hoffmann-La Roche Ltd. 2003. Roche framework for discussing and resolving ethical issues in human subject research. Available at: http://www.roche.com/process_resolving_ethical_issues_in_clinical_trials.pdf (accessed October 15, 2013).

Farsides, C. 2003. The ethics of clinical research. In *Manual for research ethics committees*, ed. S. Eckstein, 5–14. Cambridge, UK: Cambridge University Press.

Greenberg, R. A., K. W. Anstey, R. Macri, A. Heesters, S. Bean, and S. R. Zlotnik. 2014. Bioethics consultation practices and procedures: A survey of a large Canadian community of practice. *Healthcare Ethics Committee Forum* 26(2): 135–146.

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. 1996. ICH harmonised tripartite guideline: Guideline for good clinical practice E6(R1). Available at: http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6_R1/Step4/E6_R1_Guideline.pdf (accessed July 17, 2012).

McCormick, J. B., R. R. Sharp, A. L. Ottenberg, C. R. Reider, H. A. Taylor, and B. S. Wilfond. 2013. The establishment of research ethics consultation services (RECS): An emerging research resource. *Clinical and Translational Science* 6(1): 40–44.

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. 1978. *The Belmont report: Ethical principles and guidelines for the protection of human subjects in research*. Available at: <http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html> (accessed February 20, 2014).

Orr, R. D. 2009. *Medical ethics and the faith factor: A handbook for clergy and health-care professionals*. Grand Rapids, MI: Wm. B. Eerdmans.

Orr, R. D., and W. Shelton. 2009. A process and format for clinical ethics consultation. *Journal of Clinical Ethics* 20(1): 79–89.

Resnik, D. B. 2008. Research ethics consultation at the National Institute of Environmental Health Sciences. *American Journal of Bioethics* 8(3): 40–42.

Sheehan, K. B. 2001. E-mail survey response rates: A review. *Journal of Computer-Mediated Communication* 6(2). doi: 10.1111/j.1083-6101.2001.tb00117.x

Taylor, H. A., and N. E. Kass. 2009. Research ethics consultation at the Johns Hopkins Bloomberg School of Public Health. *IRB: Ethics & Human Research* 31(2): 9–14.

Van Campen, L. E., M. L. Klopfenstein, and D. G. Therasse. 2012. Development of a bioethics framework for pharmaceutical human biomedical research. Poster presented at the 14th annual meeting of the American Society for Bioethics and Humanities, Washington, DC, October.

World Medical Association (WMA). 2008. *Declaration of Helsinki: Ethical principles for medical research involving human subjects*. Available at: <http://www.wma.net> (accessed January 19, 2012).