ENCEPP/SDPP/14789

NON-INTERVENTIONAL STUDY (NIS) PROTOCOL

Study information

Title	Healthcare Professional and Patient Surveys to Assess the Effectiveness of Additional Risk Minimization Measures for Concentrated Insulin Lispro (Humalog® KwikPen® 200 units/mL)
Protocol version identifier	Version 1.0
Date of last version of protocol	20MAY2016
Active substance	Insulin Lispro
Medicinal product	Humalog® KwikPen® 200 units/mL
Research question and objectives	This study aims to evaluate the impact of the additional risk minimization measures on healthcare professional and patient understanding and behavior regarding the risk of hypoglycemia and/or hyperglycemia due to medication errors associated with administration of Humalog® KwikPen® 200 units/mL.
Country of study	United States (US)

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1. LIST OF ABBREVIATIONS

Abbreviation	Definition
aDCT	annotated Data Collection Tool
CATI	Computer-Assisted Telephone Interviewing
CFR	Code of Federal Regulation
CIs	Confidence Intervals
DHPC	Direct Healthcare Professional Communication
EDC	Electronic Data Capture
IRB	Institutional Review Board
Lilly	Eli Lilly and Company
FDA	(US) Food and Drug Administration
HCPs	Healthcare Professionals
NIS	Non-Interventional Study
PBM	Pharmacy Benefits Manager
Pen	Multi-dose pen-injector device
SDLC	System Development Life Cycle
SERP	Safety Event Reporting Procedure
SOPs	Standard Operating Procedures
T2DM	Type 2 Diabetes Mellitus
UAT	User Acceptance Testing
UBC	United BioSource Corporation
US	United States
USPS	United States Postal Service

2. RESPONSIBLE PARTIES

Principal Investigator(s) of the Protocol

Name, degree(s)	Title	Affiliation	Address
Ayad Ali, PhD	Pharmacoepidemiologist	Eli Lilly and Company	Eli Lilly and Company Lilly Corporate Center Indianapolis, IN 46285, USA

3. MILESTONES

Milestone	Planned date
Start of data collection	Estimated August 2016
End of data collection	Estimated November 2016

3.1. Rationale and Background

Diabetes, especially type 2 diabetes mellitus (T2DM), is increasing in global prevalence and associated economic and humanistic burdens. Despite tangible improvement in disease management, poor glycemic control remains a problem for individuals with diabetes (Inzucchi et al, 2012). Diabetes management guidelines recommend early initiation of insulin therapy in individuals with poor T2DM control or those with poor response to other anti-diabetes medications (Petznick A, 2011; ADA, 2014). In addition, insulin resistance and progressive loss of pancreatic beta-cell function are prodromal features of T2DM, which partially contribute to the need for high-dose insulin therapy—worldwide, about 30% of patients using basal insulin require more than 60 units daily (Gough et al, 2013), and approximately half of patients with T2DM will eventually require insulin to manage their diabetes (Jabbour, 2008).

Hypoglycemia is an identified risk of insulin therapy, and compared to other anti-diabetes medications, hypoglycemia risk is the highest with insulin (Maria Rotella et al, 2013). Hypoglycemia may occur due to low carbohydrate intake, alcohol consumption, exercise, or stress. On the other hand, failure to receive an adequate amount of insulin can result in hyperglycemia and poor diabetes control (Cornish, 2014). Hyperglycemia may occur due to excessive carbohydrate intake, less than planned exercise, illness or stress. Additionally, medication errors may contribute to these two conditions.

Insulin formulations are listed among the high-alert medications that have the potential to cause significant patient harm due to medication errors—in hospital setting, about 24% of insulin errors contributed to patient harm and 33% of deaths due to medication errors were attributed to insulin therapy (Cobaugh et al, 2013). Insulin medication errors occur across the continuum of medication-use process; however, prescribing and administration related medication errors are most common (Cobaugh et al, 2013). Medication errors involving insulin may include inadvertent interchange between insulin strengths or formulations, incorrect dosage, or incorrect use of pen-injector devices. These errors may result in hyper/hypoglycemia.

Humalog U-200 KwikPen is a prefilled and multi-dose pen-injector device (pen) that delivers insulin lispro by subcutaneous injection to improve glycemic control in adults and children with diabetes mellitus. Compared to Humalog U-100 KwikPen, it contains the same number of units of insulin lispro in half the volume. Despite warning messages on the pen and in the instructions for use, results from Human Factors studies performed in the United States (US) showed that a small percentage of patients may choose to withdraw insulin from the pen cartridge with a syringe if faced with device malfunction. Anecdotal information also indicates that patients may transfer insulin lispro from the pen cartridge into an insulin pump. Because of these data and to further optimize the benefit-risk balance of the presentation, additional Risk Minimization Measures beyond routine risk minimization measures (are being implemented, including communications to Healthcare Professionals (HCPs) and patients to minimize the risk of hyperglycemia and/or potentially hypoglycemia associated with insulin transfer from the pen cartridge to an alternative administration device without concentration adjustment and dose adjustment when transferring from Humalog U-100 KwikPen to Humalog U-200 KwikPen.

The additional Risk Minimization Measures will include a Direct Healthcare Professional Communication (DHPC) that will be distributed to pharmacists and prescribers (endocrinologists and mealtime insulin prescribing primary care physicians, nurse practitioners, and physician’s

assistants). A patient communication document will be distributed in the single pen product sample packages that are routinely provided by HCPs to patients who have been newly prescribed Humalog U-200 KwikPen.

4. RESEARCH QUESTIONS AND OBJECTIVES

The primary study objective is to evaluate the impact of the risk minimization measures on HCP and patient understanding regarding the risk of hypoglycemia and/or hyperglycemia due to medication errors associated with administration of Humalog U-200 KwikPen as communicated through the risk minimization measures.

The secondary objective is to evaluate behavior of HCPs and patients regarding the risk of hypoglycemia and/or hyperglycemia due to medication errors associated with administration of Humalog U-200 KwikPen as communicated through the risk minimization measures.

Specifically, this protocol refers to the surveys that are designed to assess the effectiveness of communications to HCPs and patients by assessing their understanding of the risks and safe use of Humalog U-200 KwikPen which were communicated through risk minimization measures including the following key safety messages:

HCPs:

- It is not necessary to adjust the insulin dose when switching from one strength of Humalog to the other
- Humalog U-200 KwikPen should not be transferred from the KwikPen to a syringe or insulin pump
- It is necessary to specify the Humalog strength on prescriptions
- It is necessary that patients always have a backup pen

Patients:

- It is not necessary to adjust the insulin dose when switching from one strength of Humalog to the other
- Humalog 200 units/mL should not be transferred from the KwikPen to a syringe as this could result in SEVERE OVERDOSE
- It is always necessary to carry a backup pen

The surveys are also designed to answer the following process research questions to assess the effectiveness of communications to HCPs and patients through the risk minimization measures. By testing a representative population about their knowledge and understanding of key safety message themes, we can generalize the:

HCPs:

- Extent of understanding of the key safety messages for Humalog U-200 KwikPen, as communicated through the DHPC (Were the key safety messages communicated in the DHPC understood by the HCP?)

- Extent of discussion between HCPs and patients when initially prescribing or dispensing Humalog U-200 KwikPen (Did the HCP convey the key safety messages in the label and DHPC to patients when they received their initial prescription of Humalog U-200 KwikPen?) with reference to the key safety messages.

Patients:

- Extent of understanding of the key safety messages for Humalog U-200 KwikPen, as communicated through risk minimization measures (Were the key safety messages in the patient communication understood by the patient?)
- Extent of recall/receipt of the patient communication in the patient sample upon first prescription of Humalog U-200 KwikPen (Does the patient recall receiving the patient sample which included the patient communication document?)
- Extent of key safety message consideration by patients during administration of Humalog U-200 KwikPen (Will the patient follow the key safety messages communicated during administration of Humalog U-200 KwikPen?)

5. RESEARCH METHODS

5.1. Study Design

This study will be observational and cross-sectional in design. Separate surveys will be administered to HCPs involved in the treatment and management of patients with diabetes and to patients with diabetes who have been prescribed Humalog U-200 KwikPen. The study has been designed and will be executed and analyzed in collaboration with United BioSource Corporation (UBC). The surveys have been developed to enable the study objectives to be met.

Qualitative Research (also known as User Testing) was performed on each survey with a sample of 12 HCPs and 9 patients. The Qualitative Research procedure was designed to assess comprehension among patients regarding the words and phrases used in select survey questions and response options. Qualitative Research also assessed the clarity of the survey questions as presented to HCPs and the interest and acceptance of the surveys among all prospective respondents, flow and ease of completing the surveys, and preferred modes of administration. Findings and recommendations from Qualitative Research have been incorporated into the surveys

Assessment of the additional risk minimization measures in the participating samples will be used to determine whether the target populations are aware of and adherent to the key safety message themes regarding the risk of hypoglycemia and/or hyperglycemia attributed to medication errors or misuse associated with the administration of Humalog U-200 KwikPen. All statistical analyses will be descriptive, i.e., no formal hypothesis will be tested.

HCPs:

HCPs will be identified through Lilly's list of HCPs who were targeted for the DHPC. Surveys targeting eligible HCPs will be administered via two modalities: 1) Internet, which will allow respondents to participate at a time and location that is convenient for them, or 2) by telephone to allow participation by respondents who may not have Internet access. Each invitation will

include information on how to access the online survey and provide the toll-free number for accessing the telephone survey. Both modalities will offer the same survey.

All HCPs who complete all survey questions and who provide their contact information will be compensated $100 in the form of a gift card to thank them for their time and effort. HCPs who choose to participate and complete a survey and are licensed and practice in Massachusetts, Minnesota, Vermont, or the District of Columbia will not receive compensation in accordance with state laws. HCPs will be informed that if they are from these states and are eligible to participate, they will not receive compensation for their time or effort. The mailing will also include a Thank You Letter, a copy of the DHPC on the correct use of Humalog U-200 KwikPen (insulin lispro) and a copy of the correct answers to key safety message questions. Respondent-identifying information will be collected by UBC for the purposes of providing payment only.

Patients:

Patients will be identified through a Pharmacy Benefits Manager (PBM) partner, which will provide broad demographic coverage and include patients in 50 states and the District of Columbia. Surveys targeting eligible patients will be administered via two modalities: 1) the Internet, which will allow respondents to participate at a time and location that is convenient for them, or 2) by telephone, which will allow participation of respondents who do not have Internet access or who are not computer literate. Each invitation will include information on how to access the online survey and will provide the toll-free number for accessing the telephone survey. Both modalities will offer the same survey.

All respondents who complete a survey and who provide their contact information will be provided $20 in the form of a gift card to thank them for their time and effort. The mailing will also include a Thank You Letter, a copy of the Patient Information Letter/*IMPORTANT SAFETY INFORMATION* for Humalog U-200 KwikPen (insulin lispro) and a copy of the correct answers to key safety message questions. Respondent-identifying information will be collected by UBC for the purposes of providing payment only.

5.2. Populations

HCPs:

HCPs involved in the treatment and management of patients with diabetes who are aware of the insulin product Humalog U-200 KwikPen will be eligible. The respondent population will include a mix of HCPs who have and have not prescribed Humalog U-200 KwikPen. HCPs who have ever worked for or who have family members who have ever worked for Eli Lilly and Company (Lilly), UBC, or the FDA (Food and Drug Administration) will be excluded. Screening questions will be used to determine respondent eligibility.

Patients

Patients will be identified through a PBM partner, which will provide broad demographic coverage and include patients in 50 states and the District of Columbia. Leveraging this partner, a list of patients who are 18 years or older, have diabetes and have filled/refilled at least one (1) prescription for Humalog U-200 KwikPen in the past 90 days will be eligible to participate. Those who have ever worked for or who have family members who have ever worked for Lilly,

UBC, or the FDA will be excluded. Screening questions will be used to determine respondent eligibility.

5.3. Study Endpoints

The additional Risk Minimization Measures will be considered effective if the majority of respondents demonstrate they are aware of the key safety messages communicated.

HCPs:

- Demonstrating that they understand the key safety messages communicated in the DHPC.
- Reporting they discuss the safe use of the product as defined in the product label and DHPC to their patients who are receiving their first prescription of Humalog U-200 KwikPen.

Patients:

- Demonstrating that they understand the key safety messages communicated about Humalog U-200 KwikPen.
- Reporting that they follow the key safety messages during administration of Humalog U-200 KwikPen.

All statistical analyses will be descriptive, i.e., no formal hypothesis will be tested.

5.4. Setting

The assessment surveys will be executed and the analysis will be completed within 18 months from product launch.

HCPs:

Eligible HCPs will receive an invitation letter (APPENDIX I.2) via email if an email address is available, or a letter via the United States Postal Service (USPS). The invitation letter will include: an overview of the rationale for the survey, information on how to access the survey online and by telephone, and a unique User Identification to ensure that the invitation is used only once. For telephone interviews, a trained interviewer, working from a computer-assisted telephone interviewing (CATI) script, will read questions or statements to the HCP. The letter will also contain a unique code that the respondent must provide when accessing the survey via the Internet or telephone. For telephone interviews, a trained interviewer, working from a computer-CATI script, will read questions or statements to the HCP. The average survey is expected to take approximately 15 minutes to complete.

A random sample of HCPs will be recruited to participate in the survey based on the list of HCPs to whom Lilly has provided a DHPC letter. The recruitment letter will indicate that participants will be compensated $100 for their time and effort in completing the survey with the exception of HCPs who are licensed and practice in Minnesota, Vermont, Massachusetts or the District of Columbia in accordance with state laws. HCPs from these states can elect to participate however they will not be paid. Respondent-identifying information will be collected for the purposes of providing payment.

The response rate will be monitored throughout the data collection period. Reminder notices will be sent via email and or via the USPS. Additional recruitment methods may be explored during survey execution if necessary to achieve a total of 280 completed surveys.

Patients:

Eligible patients will receive an invitation letter (APPENDIX I.4) mailed by the PBM directly to the patient via the USPS. The invitation letter will indicate that participants will be compensated $20 for their time and effort in completing the survey and will also include an overview of the rationale for the survey, information on how to access the survey online and by telephone, and a unique User Identification to ensure that the invitation is used only once. For telephone interviews, a trained interviewer, working from a CATI script, will read questions or statements to the patient. The letter will also contain a unique code that the respondent must provide when accessing the survey via the Internet or telephone. The average survey is expected to take approximately 15 minutes to complete.

The response rate will be monitored throughout the data collection period. If necessary, reminder notices will be sent to patients who have been invited to participate but have not responded. Additional recruitment methods may be explored prior to and or during survey launch if necessary to achieve a total of 280 completed surveys.

5.4.1. Inclusion criteria

HCPs must meet the following criteria to be eligible for inclusion in the survey:

- HCPs are aware of the insulin product Humalog U-200 KwikPen; and
- HCPs are involved in the treatment and management of patients with diabetes.

Patients must meet all of the following criteria to be eligible for inclusion in the survey:

- Patients are 18 years or older;
- Patients have diabetes; and
- Patients have filled at least one (1) prescription of Humalog U-200 KwikPen within the past 90 days.

5.4.2. Exclusion criteria

HCPs meeting any of the following criteria will not be included in the survey:

- HCPs who are not involved in the management of patients with diabetes
- HCPs who have ever worked for or who have had family members who have ever worked for Lilly, UBC, or the FDA will be excluded.

Patients meeting any of the following criteria will not be included in the survey:

- Patients with diabetes who have not been prescribed Humalog U-200 KwikPen
- Patients who have ever worked for or who have had family members who have ever worked for Lilly, UBC, or the FDA will be excluded.

5.5. Variables

The surveys will collect participants' understanding of the key safety messages in the risk minimization communication and information about potential behavior. Additionally, the HCP survey will collect information on demographic characteristics that include age, gender, geographical location, HCP specialty, and practice information. HCP-identifying information will be collected for the purposes of providing payment for participation where applicable. The patient survey will collect a variety of respondent demographic characteristics that include age, gender, geographical location, and their length of experience with any insulin therapy and Humalog U-200 KwikPen.

5.6. Data sources

In this survey, the data source for HCPs will be Lilly's list of HCPs who received the DHPC. From this data source HCPs will be invited to participate in the survey. The data source for patients will be the PBM's prescription data identifying those patients who have filled/refilled a prescription of Humalog U-200 KwikPen within 90 days prior to survey launch.

Structured questionnaires (APPENDIX I.1 and APPENDIX I.3) comprised of closed-ended questions or statements with multiple response choices (i.e., questions or statements asking the respondents to choose from a defined list of responses) will be used to collect the survey data. The surveys will collect data on respondent characteristics and their responses to the risk understanding questions. The data collected from the surveys will be used to inform the evaluation of the effectiveness of the risk minimization measures.

Each survey will begin with a screening module with questions to confirm eligibility. Depending on the answers to the screening questions, survey participation will either be terminated or continued. If ineligible, the respondent is immediately notified with a "thank you" message that survey participation has ended. If eligible, the respondent is allowed to continue survey participation.

HCPs:

Screening questions:

- Agreement to participate
- Involved in the management of patients with diabetes
- Employment by Lilly, UBC, or the FDA
- Awareness of Humalog U-200 KwikPen

Data on demographic characteristics:

- Age
- Gender
- Role at facility
- Facility type
- State of practice

- HCP medical specialty (e.g., endocrinology, primary care)
- Number of years practicing medicine/nursing
- Number of Humalog U-200 KwikPen-treated patients the HCPs prescribed to or managed in the 12 month period preceding the survey (self-reported)

Data pertaining to evaluation of the effectiveness of the risk minimization measures:

The survey includes questions/statements that will assess the understanding or the risks and associated behavior of the HCPs to minimize these risks. The understanding level and behaviors will be analyzed using descriptive statistics and confidence intervals (CIs) and will be used to determine the effectiveness of the risk minimization measures:

- Awareness of the DHPC on the correct use of Humalog U-200 KwikPen
- Understanding of the key safety messages
- Self-reported practices with respect to communication of the key safety messages in clinical practice

Patients:

Screening questions:

- Agreement to participate
- Diagnosis of diabetes
- Filled a prescription for Humalog U-200 KwikPen within the past 90 days prior to survey launch
- 18 years or older
- Employment by Lilly, UBC, or the FDA

Data on demographic characteristics:

- Age
- Gender
- State
- Employment status
- Length of time with diabetes
- Length of time on any insulin therapy
- Length of time on Humalog U-200 KwikPen
- Length of time on mealtime Insulin used prior to Humalog U-200 KwikPen

Data pertaining to evaluation of the effectiveness of the risk minimization measures:

The survey includes questions/statements that will assess the risk understanding and behavior of patients. The understanding level and behaviors will be analyzed using descriptive statistics and CIs and will be used to determine the effectiveness of the risk minimization measures:

- Awareness of the Important Safety Information for Humalog U-200 KwikPen
- Receipt of or access to the Important Safety Information
- Understanding of the key safety messages
- Behavior with respect to the key safety messages

5.6.1. Data collection process

The Internet survey will be self-administered. For the telephone survey, a trained interviewer from the Survey Coordinating Center will conduct the telephone interviews using a CATI program and enter participant responses directly into the Electronic Data Capture (EDC) System while in conversation with the respondent. Questions are programmed to ensure that they are asked in the appropriate sequence and skip patterns are clearly indicated. Respondents cannot go back to a question once the question has been answered and they cannot skip ahead. Statements requiring response and response options presented in a list are randomized to minimize positional bias.

5.7. Study size

The target sample sizes for the HCP and patient populations are 280 completed surveys for each population. The size of the sample was determined based on both practical and statistical considerations. There is no target comprehension rate specified *a priori*. A sample of 280 completed surveys for both HCPs and patients will allow estimation of the comprehension rate for each key safety message with a moderately high degree of precision. The table below shows the precision of the estimates for level of understanding using two-sided 95% CIs obtained with the sample size of 280 completed surveys. The noted CIs are used to indicate that for any survey-estimated rate of understanding, the true population rate of understanding is at least as high as the lower limit of the 95% CI and may be as high as the upper limit of the 95% CI.

Equation 1

$$95\%CI = Response\ Rate \pm 1.96 \left\{\sqrt{\left[\frac{Response\ Rate(1-Response\ Rate)}{Sample\ Size}\right]}\right\}$$

Table 1 Sample size calculations

Sample Size	Observed Response Rate* (e.g. Knowledge)	2-Sided 95% CI		
		Half-width	Lower Limit	Upper Limit
280	50%	5.9%	44.1%	55.9%
	60%	5.7%	54.3%	65.7%
	70%	5.4%	64.6%	75.4%
	80%	4.7%	75.3%	84.7%
	90%	3.5%	86.5%	93.5%

*Percentage of responders who correctly answered a question.

5.8. Data management

All data collected during the survey will be held confidentially by UBC. The EDC system used for data collection encrypts all respondent-identifying information, and respondent identifiers are stored separately from the survey responses. No identifiable information will be required from any respondent, but will be collected if they are eligible and wish to receive payment.

The survey is programmed to ensure Internet and telephone respondents cannot skip ahead and will only allow for missing data when caused by skip patterns.

Skip logic as well as the ability to mark only one response or multiple responses are part of the programming for the survey administration and minimize the occurrence of data entry errors. There will be no queries to respondents for this project.

5.9. Data analysis

Data collected from the survey will be reported as descriptive statistics. Frequency distributions with 95% CIs will be calculated for respondent responses to all questions that address the survey objectives. Responses to each question relating to the key safety messages will be categorized as “Correct response” and “Incorrect response”. “I don’t know” is categorized as an incorrect response unless otherwise specified.

In addition to the overall analysis, survey data will be analyzed to determine if there are any differences for HCPs, by medical specialty.

The following will be reported as part of the analysis:

HCPs:

Survey administration

- The number of survey invitations issued by method of distribution and specialty

- The number of survey invitations returned due to incorrect mailing address of HCPs invited to participate in the survey
- The number of HCPs who responded to the invitation to participate in the survey
- The number of HCPs eligible for participation in the survey
- The number of ineligible HCPs along with the reasons for ineligibility
- The number of eligible HCPs who completed the survey

Demographic characteristics of participants

- Distribution of participants by age groups
- Distribution of participants by gender
- Distribution of participants by practice setting
- Distribution of HCP by state
- Distribution of participants by medical specialty
- Distribution of participants by years in medical practice
- Distribution of participants by number of patients treated with Humalog U-200 KwikPen

Responses to questions pertaining to the survey objectives:

- Awareness of the DHPC on the correct use of Humalog U-200 KwikPen
- Understanding of the key safety messages
- Self-reported practices with respect to communication of the key safety messages in clinical practice

Patients:

Survey administration

- The number of invitations distributed
- The number of survey invitations returned due to incorrect mailing address of patients invited to participate in the survey
- The number of patients who responded to the invitation to participate in the survey
- The number of patients eligible for participation in the survey
- The number of ineligible patients along with the reasons for ineligibility
- The number of eligible patients who completed the survey

Demographic characteristics of participants

- Distribution of participants by age groups
- Distribution of participants by gender
- Distribution of patient by state

- Distribution of participants by years with diabetes
- Distribution of participants by length of time treated with any injectable insulin therapy
- Distribution of participants by length of time treated with Humalog U-200 KwikPen
- Distribution of participants by length of time of prior insulin use prior to Humalog U-200 KwikPen

Patient responses to questions pertaining to the survey objectives:

- Awareness of the Important Safety Information for Humalog U-200 KwikPen
- Receipt of or access to Important Safety Information
- Understanding of the key safety messages
- Self-reported practices with respect to the key safety messages

5.10. Quality control

Data will be collected using a secure online EDC system that has been developed and fully validated. A rigorous System Development Life Cycle (SDLC) is used for validation that complies with 23 internal IT Standard Operating Procedures (SOPs) of UBC. Unit testing and formal validation occur on all appropriate systems and components during the build stage. The SDLC is fortified with SOPs addressing validation for all clinical and risk minimization-related applications. The Internet-based repository will be used to store survey data and other relevant program information. The system is 21 CFR (Code of Federal Regulations) Part 11 compliant for the entry, storage, manipulation, analysis and transmission of electronic information. This platform ensures compliance with all relevant regulatory guidelines. Respondent-identifying information is stored separately from survey data.

Programming will be reviewed by Quality Control and simulated users [User Acceptance Testing (UAT)] prior to implementation.

At the completion of data collection, data will be extracted from the EDC and mapped to SAS datasets (SAS V9.1.3 or higher) as defined in the application Data Collection Tools (aDCTs). The mapping of raw data will be validated, as will the programming of the analysis datasets created from the raw EDC SAS datasets. The Analysis SAS datasets are used to populate analysis tables that are programmed by using SAS according to the survey analysis plan. The final datasets and table output will be independently validated using SAS, and reviewed by the Quality Assurance Team.

The UBC has an Information Technology Quality Assurance Group that is responsible for managing and overseeing system/application development and validation, as well as related compliance functions.

5.11. Limitations of the research methods

The participants will be self-selected since they will voluntarily respond to the invitation to participate. The survey recruitment strategies will include a random sample of HCPs who received educational outreach, which should be generalizable to the overall HCP population who are educated about the use of Humalog U-200 KwikPen.

Patients will be recruited via the PBM database and will be identified as those patients who have filled/refilled a prescription for Humalog U-200 KwikPen.

Additionally, inherent in survey research is the reliance on the respondent's recall for whether or not the risk minimization communication was received in order to evaluate the scope of risk minimization measures. If the respondent says she/he did not receive the communication, the risk minimization program is evaluated as not optimally disseminating material. It is possible, however, that respondents may simply not recall receiving the tools that were, in fact, received. It is also possible that they have acceptable understanding of the risks and appropriate behaviors despite not receiving or recalling receipt of the risk minimization measure-specific communication. All data from the survey are self-reported and therefore susceptible to possible reporting bias. This is also applicable to the patients' self-reporting of their practice behaviors to minimize the risks. There may be discrepancies between what respondents report about their practices and their actual behaviors.

5.11.1. Controls to minimize bias

A number of controls will be in place to ensure the survey is conducted in a professional manner and to minimize bias, including the following:

- Lists of response options will be randomized to minimize the potential for positional bias.
- The Internet and telephone surveys will be programmed to ensure that questions are asked in the appropriate sequence and all questions will be presented in a standard order to reduce exposure bias. Respondents cannot skip ahead or go back to a question once the question has been answered. All questions presented must be answered in order to complete a survey. Not all questions may be presented due to skip logic within the survey.
- Respondents will be provided with a unique code during the recruitment process and will then be asked to provide the unique code in order to gain access to the Internet-based and telephone administration systems. The code will be inactivated after use to minimize exposure bias and fraud.

6. PROTECTION OF HUMAN SUBJECTS

6.1. Personal Information and Consent

All data collected during the survey will be held confidential by UBC and used only for the purposes stated in the survey instructions. Respondent names and addresses are collected for the purposes of mailing a thank you letter and payment, if applicable, after the survey is completed. The EDC system used for data collection encrypts all identifiable information, and respondent identifiers are stored separately from the survey responses.

By answering the first question of the survey ("*Do you agree to take part in this survey about Humalog® KwikPen®, 200 units/mL (Humalog® U-200 KwikPen®?*") after reading the introductory message ("Preamble 1"), respondents are acknowledging informed consent for participation in the research study.

If, during survey completion, UBC project personnel are made aware of a safety event, the UBC project personnel will follow the reporting structure described in Section 7. The respondent will

be asked for consent to allow their contact information to be provided to Lilly, so that Lilly may contact them for additional information. If the consent is not granted, UBC personnel will report the Safety Event with the information provided by the respondent.

6.2. Respondent withdrawal

Respondents can decline to participate or stop taking the survey at any time. Only completed surveys that include all questions answered that were required to be presented for participation will be included in the analysis.

Respondents will be informed when they access the survey that they may be contacted if there are any questions about their survey responses. Respondents will be informed that their answers to the survey questions will not affect their ability to receive Humalog U-200 KwikPen.

6.3. Central Institutional Review Board (IRB)

This protocol was reviewed and approved by a central IRB before administration of the survey.

7. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

This study does not involve data collection on clinical endpoints on individual respondents.

The Internet survey does not include questions that could potentially identify a safety event, nor does it provide a free text field where study participants could specify information that may constitute a safety event (defined as an adverse event, product complaint, or other reports; e.g. overdose, abuse, misuse, off label use, pregnancy exposures, breast feeding exposures, lack of drug effect, medication error and suspected transmission of infectious disease). Free text fields are available in the survey to only collect contact information to provide payment. However, it is possible that while in conversation with UBC Personnel, a telephone respondent may provide information that could constitute a Safety Event.

Trained UBC Personnel will record any reference to a Safety Event in temporal association with Humalog U-200 KwikPen as stated (verbatim) in the UBC Humalog U-200 KwikPen Safety Event Form, along with the respondent's contact information, if consent to provide contact information is given. The respondent will also be informed that someone from Lilly may contact them to obtain additional information about the event. If consent is not granted, UBC personnel will report the Safety Event with the information provided by the respondent. Information on all reports that may constitute a Safety Event will be forwarded to Lilly as described in the Safety Event Reporting Procedure (SERP). Additional detail regarding processes for adverse event reporting will be specified in the SERP. Study personnel are requested to report suspected adverse reactions with Lilly drugs not under evaluation and with any non-Lilly drugs to one appropriate party to avoid duplication, (for example, regulators or Lilly) as they would in normal practice as required by applicable laws, regulations and practices.

8. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

A final report for each stakeholder group describing the survey objectives, detailed methods, results, discussion, and conclusions will be developed at the end of the survey.

9. REFERENCES

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ANNEX 1. LIST OF STAND-ALONE DOCUMENTS

Number	Document reference number	Date	Title
1	Appendix I.1		HCP Survey
2	Appendix I.2		Survey Invitation letter for HCPs
3	Appendix I.3		Patient Survey
4	Appendix I.4		Survey Invitation letter for Patients
5	Appendix I.5		Direct Healthcare Professional Communication on the correct use of Humalog KwikPen®, 200 units/mL (Humalog® U-200 KwikPen®)
6	Appendix I.6		Patient Information Letter/*IMPORTANT SAFETY INFORMATION* for Humalog® U-200 KwikPen® (insulin lispro)

APPENDIX I.1 HEALTHCARE PROFESSIONAL SURVEY

SURVEY LEGEND

- **[PROGRAMMER]** is used to indicate directions to the programmer and is set in bold, red, uppercase letters between square brackets.

- **(INTERVIEWER)** is used to indicate directions to the telephone interviewer and is set in bold, blue, text between parentheses. This text appears when content is to be administered by telephone only (for example, spontaneous AE reporting).

- **[ONLINE]** indicates a question is worded specifically for administering the survey online.

- **[TELEPHONE]** indicates a question/section is worded specifically for administering the survey over the telephone.

- **[BEGIN SURVEY CONTENT]** and **[END SURVEY CONTENT]** are used to indicate to the programmer the type of survey administration and the beginning and end of the survey or sections within the survey content.

- **[TERMINATE]** is displayed next to responses that should cause the survey to end. The following termination language will be programmed into the survey or read by the interviewer.

  Thank you very much for your time today. Based on your answer, you are not eligible to take this survey. We appreciate your interest in the survey.

- **[RANDOMIZE LIST]** is inserted before questions to indicate to the programmer that the responses should be randomized. Responses such as “I don’t know,” “Prefer not to answer” or “None of the above” will always appear at the end of the randomized responses.

- **[GO TO Qx]** (skip logic) is inserted after a response to indicate to the programmer that the survey should skip to the indicated question (for example, **[GO TO Q17]** skips to question 17). If no skip logic is indicated the survey continues to the next question in the sequence.

- **[MULTILINE INPUT]** indicates to the programmer that multiple lines should be provided for data entry (for example, two address lines).

- **[FREE TEXT]** indicates to the programmer that one line should be provided for data entry.

SURVEY LEGEND

- **[DROP-DOWN LIST INPUT WITH STATES TABLE]** indicates to the programmer that the response should be a drop-down list containing the states in the table below.

Alabama	Georgia	Massachusetts	New York	Tennessee
Alaska	Hawaii	Michigan	North Carolina	Texas
Arizona	Idaho	Minnesota	North Dakota	Utah
Arkansas	Illinois	Mississippi	Ohio	Vermont
California	Indiana	Missouri	Oklahoma	Virginia
Colorado	Iowa	Montana	Oregon	Washington
Connecticut	Kansas	Nebraska	Pennsylvania	West Virginia
Delaware	Kentucky	Nevada	Rhode Island	Wisconsin
District of Columbia	Louisiana	New Hampshire	South Carolina	Wyoming
Florida	Maine	New Jersey	South Dakota	
	Maryland	New Mexico		

- The following is used to categorize survey populations into standard geographic regions but it is not displayed in the survey.

  Geographic Distribution (based on address) [1]: Northeast, Midwest, South, and West regions

  Northeast Region
  - New England Division - ME, NH, VT, MA, RI, CT
  - Middle Atlantic Division - NY, NJ, PA

  Midwest Region
  - East North Central Division - OH, IN, IL, MI, WI
  - West North Central Division - MN, IA, MO, ND, SD, NE, KS

  South Region
  - South Atlantic Division - DE, MD, DC, VA, WV, NC, SC, GA, FL
  - East South Central Division - KY, TN, AL, MS
  - West South Central Division - AR, LA, OK, TX

  West Region
  - Mountain Division - MT, ID, WY, CO, NM, AZ, UT, NV
  - Pacific Division - WA, OR, CA, AK, HI

[1] U.S. Census Bureau, last revised Friday, 27-Jul-2001 12:59:43 EDT.

[BEGIN WELCOME PAGE]

This survey should take approximately 15 minutes to complete. If you cannot complete the survey at this time, please return when you can. Once you begin the survey you will need to answer all questions; you will not be able to access the survey again if you exit.

Consider the following important information before you start the survey: the application will time out after 30 minutes of inactivity. If your session times out, you will not be able to log back into the survey to complete it and your participation in the survey will end.

If you are ready to begin the survey at this time, please click Continue. If not, click Return Later and return to this site when it is convenient for you.

Please note: Do not use the browser's back button during this survey.

[END WELCOME PAGE]

[PROGRAMMER, DISPLAY THE FOLLOWING IN THE SURVEY PAGE HEADER: If you have questions or problems with the survey, please contact the Survey Coordinating Center at 1-1-844-810-8936.]

[BEGIN ONLINE PREAMBLE 1]

Disclaimer

Thank you for your interest in this voluntary research survey about Humalog® KwikPen®, 200 units/mL (Humalog® U-200 KwikPen®), which is being conducted by United BioSource Corporation (UBC) on behalf of the sponsor, Eli Lilly and Company (Lilly), the marketing authorization holder of Humalog® U-200 KwikPen®. This survey is voluntary and you are under no obligation to participate.

You may refuse to take part or withdraw at any time without penalty. Your answers to the questions or your decision to take part in the survey will not affect your ability to prescribe Humalog® U-200 KwikPen®. This survey should take about 15 minutes to complete.

How We Use Your Information

Your answers to the survey questions will be combined with answers from other respondents and reported in anonymous form to Lilly, and the Food and Drug Administration (FDA). Your name will not be used in any report.

If you are eligible to take the survey, complete all the survey questions, and provide your contact information, you will be compensated $100 for your time and effort. This compensation represents the fair value for your time in connection with the completion of the survey. The amount of the compensation was not determined by the volume or value of any referrals or business otherwise generated by you. Your name and address will only be used to send you the compensation after you complete the survey. Please be aware that Health Care Professionals (HCPs) who are licensed and practice in Massachusetts, Minnesota, Vermont or the District of Columbia, where compensation is not permitted, will not be eligible to receive compensation for survey participation in accordance with state laws.

How We Protect Your Privacy

We understand and respect that the privacy of your personal information is important to you. To the extent permitted by applicable laws and regulations, the records identifying you will not be made publicly available. All the information you provide will be kept strictly confidential. You will not be contacted for marketing purposes based on your personal information or your answers to the survey. Neither Lilly nor its contractors will sell, transfer, or rent your information. Your privacy will be

protected; however, research survey records may be inspected by the FDA or other regulatory agencies. Should a Safety Event in a specific patient be identified, we are required to report this even if it has already been reported to the manufacturer or the regulatory authority. Your choice to allow Lilly to use your answers to the survey questions is entirely voluntary but necessary to receive payment for participation.

The aggregate results of the survey maybe presented at meetings or in articles written about the survey (publications). If the results of the survey (including your research information) are published, your identity will remain confidential.

How to Learn More about This Survey

If you have questions about or problems with the survey, please contact the Survey Coordinating Center at **1-844-810-8936.**

Taking the Survey

Once you have answered a question and moved on, you cannot go back and change your answers.

Thank you for your participation in this survey.

[END ONLINE PREAMBLE 1]

[BEGIN TELEPHONE PREAMBLE 1]

Disclaimer

Thank you for your interest in this voluntary research survey about Humalog® KwikPen®, 200 units/mL (Humalog® U-200 KwikPen®) , which is being conducted by United BioSource Corporation (UBC) on behalf of the sponsor, Eli Lilly and Company (Lilly), the marketing authorization holder of Humalog® U-200 KwikPen®. This survey is voluntary and you are under no obligation to participate.

This survey should take approximately 15 minutes to complete. If you cannot complete the survey at this time, please call back when you can. Once you begin the survey you will need to answer all questions during the same telephone call; you will not be able to access the survey again if you end this call.

How We Use Your Information

Your answers to the survey questions will be combined with answers from other respondents and reported in anonymous form to Lilly, and the Food and Drug Administration. Your name will not be used in any report.

If you are eligible to take the survey, complete all the survey questions, and provide your contact information, you will be compensated $100 for your time and effort. This compensation represents the fair value for your time in connection with the completion of the survey. The amount of the compensation was not determined by the volume or value of any referrals or business otherwise generated by you. Your name and address will only be used to send you the compensation after you complete the survey. Please be aware that Health Care Professionals (HCPs) who are licensed and practice in Massachusetts, Minnesota, Vermont, or the District of Columbia, where compensation is not permitted, will not be eligible to receive compensation for survey participation in accordance with state laws.

How We Protect Your Privacy

We respect that the privacy of your personal information is important to you. To the extent permitted by applicable laws and regulations, the records identifying you will not be made publicly available. All

the information you provide will be kept strictly confidential. You will not be contacted for marketing purposes based on your personal information or your answers to the survey. Neither Lilly nor its contractors will sell, transfer, or rent your information. Your privacy will be protected; however, research survey records may be inspected by the FDA or other regulatory agencies. Should a Safety Event in a specific patient be identified, we are required to report this even if it has already been reported to the manufacturer or the regulatory authority. Your choice to allow Lilly to use your answers to the survey questions is entirely voluntary but necessary to participate.

[END TELEPHONE PREAMBLE 1]

[BEGIN SCREENING QUESTIONS]

Please provide a response to all questions and statements as they are presented.

1. Do you agree to take part in this survey about Humalog® 200 units/mL KwikPen® (Humalog® U-200 KwikPen®)?

   ○ Yes

   ○ No **[TERMINATE]**

[Q2 - FOR WAVE 2 ONLY]

2. Have you ever participated in this survey for Humalog® U-200 KwikPen® before?

   ○ Yes **[TERMINATE]**

   ○ No

   ○ I don’t know **[TERMINATE]**

3. In which state or territory do you practice and are you licensed?

   [DROP DOWN LIST INPUT WITH STATES TABLE, EXCLUDE PREFER NOT TO ANSWER]

[IF RESPONDENT ANSWERS MASSACHUSETTS, MINNESOTA, VERMONT, OR DISTRICT OF COLUMBIA, DISPLAY REMINDER MESSAGE 1 ON SAME PAGE AND GO TO Q4.]

[REMINDER MESSAGE 1]: If you practice and you are licensed in the District of Columbia, Massachusetts, Minnesota, or Vermont just a reminder that we appreciate your participation; however, no compensation for your services will be provided in accordance with local laws.

4. Please choose an option about your participation in this survey.

i. ○ I will participate in the survey and provide my contact information.

ii. ○ I will participate in the survey but choose not to be paid.

5. Are you involved in the management of patients with diabetes? This includes prescribing medications to treat diabetes or providing education to help manage diabetes.

   - ○ Yes
   - ○ No **[GO TO Q7, TERMINATE AFTER Q14]**

6. What is your role in the management of patients with diabetes?

   - ○ Physician
   - ○ Nurse Practitioner
   - ○ Physician Assistant
   - ○ Registered Nurse **[GO TO Q8]**
   - ○ Other **[GO TO Q8]**

7. What is your primary medical specialty?

   - ○ General Internal Medicine
   - ○ Endocrinology/Diabetology
   - ○ Family Medicine
   - ○ Other

8. How many years have you been in practice as a physician, physician assistant, or nurse since completing your medical/nursing education?

   - ○ Less than 5 years
   - ○ 5 – 10 years
   - ○ 11 – 15 years
   - ○ More than 15 years

9. In what type of facility do you work?

- ○ General Practice
- ○ Hospital
- ○ Other

10. Are you aware of the insulin product Humalog® U-200 KwikPen®?

- ○ Yes
- ○ No **[GO TO Q12, TERMINATE AFTER Q14]**
- ○ I don't know **[GO TO Q12, TERMINATE AFTER Q14]**

11. For how many patients have you prescribed, or managed their treatment with, Humalog® U-200 KwikPen®?

- ○ 0 **[TERMINATE AFTER QUESTION 14 IF 140 OR MORE COMPLETE RESPONDENTS HAVE ANSWERED 0, WHERE 140 IS A CONFIGURABLE NUMBER]**
- ○ 1 – 5
- ○ 6 – 10
- ○ 11 – 20
- ○ More than 20

12. Have you or any of your immediate family members ever worked for Eli Lilly and Company (Lilly), United BioSource Corporation (UBC), or the Food and Drug Administration (FDA)?

    - ○ Yes **[TERMINATE AFTER QUESTION 14]**
    - ○ No
    - ○ I don't know **[TERMINATE AFTER QUESTION 14]**

13. Which of the following groups best describes your age?

    - ○ Less than 30
    - ○ 30 – 39
    - ○ 40 – 49
    - ○ 50 – 59
    - ○ 60 – 69
    - ○ 70 or older

14. What is your gender?

    - ○ Male
    - ○ Female

[END SCREENING QUESTIONS]

[BEGIN SURVEY CONTENT]

[BEGIN PREAMBLE 2 – DISPLAY ON SAME PAGE AS NEXT QUESTION]

The following questions are about Humalog® U-200 KwikPen®.

[END PREAMBLE 2]

15. Please answer True, False, or I don't know for each of the following statements regarding Humalog® U-200 KwikPen®.

	[RANDOMIZE LIST]	**True**	**False**	**I don't know**
A	Humalog® U-200 KwikPen® is approved for transfer to syringe or pump.	○	○	○
B	The dose of insulin does not need to be converted when changing patients from one Humalog strength to the other (for example, changing a patient from Humalog U-100 units/mL to Humalog® U-200 KwikPen®).	○	○	○
C	When prescribing Humalog® U-200 KwikPen®, it is important to clearly indicate the correct strength on the prescription.	○	○	○
D	It is important to instruct your patients that they should always have a backup pen available.	○	○	○

16. Are you aware of the Direct Healthcare Professional Communication provided to you by Eli Lilly and Company on the correct use of Humalog® U-200 KwikPen® *(insulin lispro)* to minimize medication errors?

○ Yes

○ No **[GO TO Q18]**

○ I don't know **[GO TO Q18]**

17. Did you read the Direct Healthcare Professional Communication provided to you by Eli Lilly and Company on the correct use of Humalog® U-200 KwikPen® *(insulin lispro)* to minimize medication errors?

- ○ Yes
- ○ No
- ○ I don't know

18. Are you aware of the patient communication Patient Information Letter/*IMPORTANT SAFETY INFORMATION FOR* Humalog® U-200 KwikPen® *(insulin lispro)* that is included in patient sample packs of Humalog® KwikPen® provided by Eli Lilly and Company?

- ○ Yes
- ○ No **[GO TO Q20]**
- ○ I don't know **[GO TO Q20]**

19. Have you read the patient communication: Patient Information Letter/*IMPORTANT SAFETY INFORMATION FOR* Humalog® U-200 KwikPen® *(insulin lispro)* provided by Eli Lilly and Company?

- ○ Yes
- ○ No
- ○ I don't know

[DO NOT DISPLAY QUESTION 20 IF 0 IS SELECTED IN QUESTION 11]

20. Do you or another healthcare professional at your practice discuss the safe use of the Humalog® U-200 KwikPen® to patients receiving their initial prescription?

- ○ Yes
- ○ No
- ○ I don't know

[DO NOT DISPLAY QUESTION 21 IF 0 IS SELECTED IN QUESTION 11]

21. Do you or another healthcare professional at your practice discuss the Patient Information Letter/*IMPORTANT SAFETY INFORMATION FOR* Humalog® U-200 KwikPen® *(insulin lispro)* with patients at the time of initial prescription of Humalog® U-200 KwikPen®?

- ○ Yes
- ○ No
- ○ I don't know

[TELEPHONE: BEGIN SAFETY EVENT – KEEP ON ONE PAGE]

(INTERVIEWER: Please record if respondent spontaneously reported a safety event or product complaint during the course of this interview.)

- ○ Yes
- ○ No

Enter Safety Event or Product Complaint Verbatim

[MULTILINE INPUT]

(INTERVIEWER: Indicate to the respondent that someone may call back to ask more questions about the adverse event or product complaint that was reported.)

[TELEPHONE: END SAFETY EVENT]

[BEGIN CLOSING 1]

[DISPLAY CLOSING 1 IF QUESTION 4= i.]

We would like to send you $100 as compensation for your time and effort as well as a copy of the Dear Healthcare Professional Communication (DHPC) for Humalog® U-200 KwikPen®, and the correct answers to key safety message questions, but need your name and address to do so. Do you agree to provide your contact information for this purpose?

- ○ Yes **[IF SELECTED, DISPLAY CONTACT INFORMATION ON SAME PAGE]**
- ○ No **[GO TO CLOSING 3]**

[END CLOSING 1]

[BEGIN CLOSING 2]

[DISPLAY CLOSING 2 IF QUESTION 3= MASSACHUSETTS, MINNESOTA, DISTRICT OF COLUMBIA OR VERMONT OR QUESTION 4 = ii OR IF NO TO CLOSING 1.]

Do you agree to give us your name and mailing address so we can send you a copy of the Dear Healthcare Professional Communication (DHPC) for Humalog® U-200 KwikPen®, as well as the correct answers to key safety message questions?

○ Yes **[IF SELECTED, DISPLAY CONTACT INFORMATION ON SAME PAGE]**

○ No **[GO TO CLOSING 3]**

[END CLOSING 2]

[BEGIN CONTACT INFORMATION]

FIRST NAME: **[FREE TEXT]**

LAST NAME: **[FREE TEXT]**

MIDDLE INITIAL: **[OPTIONAL; MUST BE 1 ALPHA CHARACTER]**

ADDRESS: **[MULTILINE INPUT]**

CITY: **[FREE TEXT]**

STATE: **[DROP-DOWN LIST INPUT WITH STATES TABLE]**

ZIP CODE: [**MUST BE 5-DIGIT NUMERIC ONLY**]

[END CONTACT INFORMATION]

[BEGIN CLOSING 3]

This completes the survey. Thank you again for your participation.

[END CLOSING 3]

[END SURVEY CONTENT]

APPENDIX I.2 HEALTHCARE PROFESSIONAL RECRUITMENT MATERIALS

[Date]

[FIRST NAME] [LAST NAME]

[Title]

[Street address]

[City, State, Post code]

Re: Invitation to Participate in Humalog® KwikPen®, 200 units/mL (Humalog® U-200 KwikPen®) Survey

Dear [FIRST NAME] [LAST NAME]:

On behalf of Eli Lilly and Company (Lilly), we would like to invite you to participate in a voluntary research survey about Humalog® U-200 KwikPen®. The survey is part of a post-marketing commitment between Lilly and the Food and Drug Administration (FDA) to assess the effectiveness of the risk minimization tools, and should take approximately 15 minutes to complete. If you are **eligible** and complete the entire survey, you will be compensated in the amount of $100 for your time and participation.

You are under no obligation to take this survey. Your answers to the questions in this survey will not affect your ability to prescribe Humalog® U-200 KwikPen®.

Please be aware that HCPs who are licensed and practice in Vermont, District of Columbia, Massachusetts, or Minnesota, where compensation for participation is not permitted, will not be eligible for compensation for survey participation in accordance with state laws. If you are licensed and practice in the District of Columbia, Massachusetts, Minnesota or Vermont, you may elect not to take the survey.

For your convenience, the survey can be completed either on-line via a secure website or over the telephone with a survey team associate. If you are interested in participating and to find out if you are eligible:

- Go to www.humalogsurveyus.com any time or
- Call **1-844-810-8936**, 8 a.m. to 8 p.m. Eastern Time, Monday through Friday

Please have this letter with you at the time you take the survey. You will be asked to provide this code prior to starting the survey: [CODE_ID]

It is recommended that you take the survey on a desktop or laptop computer. Taking the survey on mobile devices, such as smart phones, tablets, and e-notebooks, is not supported.

We respect that the privacy of your personal information is important to you. If you choose to participate in the survey, you will be asked to provide your name and address. Your name and address will only be used to send you your compensation in the amount of $100 along with a copy of the correct answers to important survey questions, and a copy of the Humalog® U-200 KwikPen® Dear Healthcare Professional Communication (DHPC).

Your answers to the survey will be combined with answers provided by others. Your name will not be used in any report. Neither taking the survey nor your answers to the questions will affect your ability to prescribe Humalog® U-200 KwikPen®. You will not be contacted for marketing purposes based on

your personal information or your answers to the survey. Your information will not be sold, transferred, or rented. Your choice to provide your information is entirely voluntary but necessary to receive your honorarium.

Thank you in advance for your participation. Your help in this survey is greatly appreciated.

Sincerely,

{Note: Signatory customized accordingly}

[Date]

[FIRST NAME] [LAST NAME]

[Title]

[Street address]

[City, State, Post code]

Re: Invitation to Participate in Humalog® KwikPen®, 200 units/mL (Humalog® U-200 KwikPen®) Survey

Dear [FIRST NAME] [LAST NAME]:

You recently received a letter informing you of a research survey about Humalog® U-200 KwikPen®. The survey is part of a post-marketing commitment between Lilly and the Food and Drug Administration (FDA) to assess the effectiveness of the risk minimization tools, and should take approximately 15 minutes to complete. If you are **eligible** and complete the entire survey, you will be compensated in the amount of $100 for your time and participation.

You are under no obligation to take this survey. Your answers to the questions in this survey will not affect your ability to prescribe Humalog® U-200 KwikPen®.

Please be aware that HCPs who are licensed and practice in Vermont, District of Columbia, Massachusetts, or Minnesota, where compensation for participation is not permitted, will not be eligible for compensation for survey participation in accordance with state laws. If you are licensed and practice in the District of Columbia, Massachusetts, Minnesota or Vermont, you may elect not to take the survey.

For your convenience, the survey can be completed either on-line via a secure website or over the telephone with a survey team associate. If you are interested in participating and to find out if you are eligible:

- Go to www.humalogsurveyus.com any time or
- Call **1-844-810-8936**, 8 a.m. to 8 p.m. Eastern Time, Monday through Friday

Please have this letter with you at the time you take the survey. You will be asked to provide this code prior to starting the survey: [CODE_ID]

It is recommended that you take the survey on a desktop or laptop computer. Taking the survey on mobile devices, such as smart phones, tablets, and e-notebooks, is not supported.

We respect that the privacy of your personal information is important to you. If you choose to participate in the survey, you will be asked to provide your name and address. Your name and address will only be used to send you your compensation in the amount of $100 along with a copy of the correct answers to important survey questions, and a copy of the Humalog® U-200 KwikPen® Dear Healthcare Professional Communication (DHPC).

Your answers to the survey will be combined with answers provided by others. Your name will not be used in any report. Neither taking the survey nor your answers to the questions will affect your ability to prescribe Humalog® U-200 KwikPen®. You will not be contacted for marketing purposes based on your personal information or your answers to the survey. Your information will not be sold, transferred, or rented. Your choice to provide your information is entirely voluntary but necessary to receive your honorarium.

Thank you in advance for your participation. Your help in this survey is greatly appreciated.

Sincerely,

{Note: Signatory customized accordingly}

[Date]

[FIRST NAME] [LAST NAME]

[Title]

[Street address]

[City, State, Post code]

Dear [FIRST NAME] [LAST NAME]:

On behalf of Eli Lilly and Company, the maker Humalog® U-200 KwikPen® of we want to thank you for taking part in the Humalog® U-200 KwikPen® Survey. To express our appreciation for your valuable time, enclosed is a $100 for your time.

Card Activation Instructions:

To prevent loss, the enclosed card is not activated. Prior to using your card, please call the Humalog® U-200 KwikPen® Coordinating Center at **1-844-810-8936** between 8:00 a.m. and 8:00 p.m. Eastern Time Monday through Friday to activate your card. Please have your card available when you make the call. Also, please read the enclosed Terms and Conditions document before using your gift card as well as the privacy policy that can be found at: http://www.ctpayer.com/downloads/privacy_policy.pdf

Please note the enclosed card needs to be activated on or before: **XX XX XXXX.**

Additionally, to ensure that survey participants have accurate information about the risks of Humalog® U-200 KwikPen®, we have also enclosed the following two documents:

1. A copy of the correct answers to the survey questions about the Humalog® U-200 KwikPen® key safety messages
2. A copy of the Humalog® U-200 KwikPen® Dear Healthcare Professional Communication (DHPC)

Sincerely,

The Humalog® U-200 KwikPen® Survey Team
1-844-810-8936
www.humalogsurveyus.com

Enclosures: Humalog® U-200 KwikPen® Dear Healthcare Professional Communication (DHPC)
Correct Answers to Key Safety Messages
Gift Card, Terms and Conditions document and Frequently Asked Questions

[Date]

[FIRST NAME] [LAST NAME]

[Title]

[Street Address]

[City, State, Post code]

Dear [FIRST NAME] [LAST NAME]:

On behalf of Eli Lilly and Company, the maker Humalog® U-200 KwikPen® of we want to thank you for taking part in the Humalog® U-200 KwikPen® Survey.

To ensure that survey participants have accurate information about the risks of Humalog® U-200 KwikPen®, we have also enclosed the following two documents:

3. A copy of the correct answers to the survey questions about the Humalog® U-200 KwikPen® key safety messages
4. A copy of the Humalog® U-200 KwikPen® Dear Healthcare Professional Communication (DHPC)

Sincerely,

The Humalog® U-200 KwikPen® Survey Team
1-844-810-8936
www.humalogsurveyus.com

Enclosures: Humalog® U-200 KwikPen® Dear Healthcare Professional Communication (DHPC)
Correct Answers to Key Safety Messages

HEALTHCARE PROFESSIONAL CORRECT ANSWER DOCUMENT

Correct Responses to PRESCRIBER Survey Questions about Key Safety Messages for Humalog® U-200 KwikPen®

Q: Please answer True, False, or I don't know for each of the following statements regarding Humalog® U-200 KwikPen®.

STATEMENT	Correct Response
Humalog® U-200 KwikPen® is approved for transfer to syringe or pump.	*FALSE*
The dose of insulin does not need to be converted when changing patients from one Humalog strength to the other (for example, changing a patient from Humalog U-100 units/ml to Humalog® U-200 KwikPen®).	*TRUE*
When prescribing Humalog® U-200 KwikPen®, it is important to clearly indicate the correct strength on the prescription.	*TRUE*
It is important to instruct your patients that they should always have a backup pen available	*TRUE*

If you have questions or are unclear about any of these responses, please refer to the Direct HealthCare Professional Communication for Humalog® U-200 KwikPen®.

PRESCRIBER Surveyresponses_ Humalog® U-200 KwikPen® v1.0 02MAY2016 Page 1 of 1

APPENDIX I.3 PATIENT SURVEY

SURVEY LEGEND

- **[PROGRAMMER]** is used to indicate directions to the programmer and is set in bold, red, uppercase letters between square brackets.

- **(INTERVIEWER)** is used to indicate directions to the telephone interviewer and is set in bold, blue, text between parentheses. This text appears when content is to be administered by telephone only (for example, spontaneous safety event reporting).

- **[ONLINE]** indicates a question/section is worded specifically for administering the survey online.

- **[TELEPHONE]** indicates a question/section is worded specifically for administering the survey over the telephone.

- **[BEGIN <Section>]** and **[END <Section>]** are used to indicate to the programmer the beginning and end of the survey or sections of text within the survey, for example, **[BEGIN PHONE PREAMBLE 1]** and **[END PHONE PREAMBLE 1]**.

- **[TERMINATE]** is displayed next to responses that should cause the survey to end. The following termination language will be programmed into the survey or read by the interviewer.

  Thank you very much for your time today. Based on your answer, you are not eligible to take this survey. We appreciate your interest in the survey.

- **[RANDOMIZE LIST]** is inserted before questions to indicate to the programmer that the responses should be randomized. Responses such as “I don’t know,” “Prefer not to answer” or “None of the above” will always appear at the end of the randomized responses.

- **[GO TO Qx]** (skip logic) is inserted after a response to indicate to the programmer that the survey should skip to the indicated question (for example, **[GO TO Q17]** skips to question 17). If no skip logic is indicated the survey continues to the next question in the sequence.

- **[MULTILINE INPUT]** indicates to the programmer that multiple lines should be provided for data entry (for example, two address lines).
- **[FREE TEXT]** indicates to the programmer that one line should be provided for data entry.

SURVEY LEGEND

- **[DROP-DOWN LIST INPUT WITH STATES TABLE]** indicates to the programmer that the response should be a drop-down list containing the states in the table below.

Alabama	Georgia	Massachusetts	New York	Tennessee
Alaska	Hawaii	Michigan	North Carolina	Texas
Arizona	Idaho	Minnesota	North Dakota	Utah
Arkansas	Illinois	Mississippi	Ohio	Vermont
California	Indiana	Missouri	Oklahoma	Virginia
Colorado	Iowa	Montana	Oregon	Washington
Connecticut	Kansas	Nebraska	Pennsylvania	West Virginia
Delaware	Kentucky	Nevada	Rhode Island	Wisconsin
District of Columbia	Louisiana	New Hampshire	South Carolina	Wyoming
Florida	Maine	New Jersey	South Dakota	
	Maryland	New Mexico		

- The following is used to categorize survey populations into standard geographic regions but it is not displayed in the survey.

  Geographic Distribution (based on address) [1]: Northeast, Midwest, South, and West regions

  Northeast Region

  – New England Division - ME, NH, VT, MA, RI, CT

  – Middle Atlantic Division - NY, NJ, PA

  Midwest Region

  – East North Central Division - OH, IN, IL, MI, WI

  – West North Central Division - MN, IA, MO, ND, SD, NE, KS

  South Region

  – South Atlantic Division - DE, MD, DC, VA, WV, NC, SC, GA, FL

  – East South Central Division - KY, TN, AL, MS

  – West South Central Division - AR, LA, OK, TX

  West Region

  – Mountain Division - MT, ID, WY, CO, NM, AZ, UT, NV

  – Pacific Division - WA, OR, CA, AK, HI

[1] U.S. Census Bureau, last revised Friday, 27-Jul-2001 12:59:43 EDT.

[BEGIN WELCOME PAGE]

This survey should take approximately 15 minutes to complete. If you cannot complete the survey at this time, please return when you can. Once you begin the survey you will need to answer all questions; you will not be able to access the survey again if you exit. Consider the following important information before you start the survey: the application will time out after 30 minutes of inactivity. If your session times out, you will not be able to log back into the survey to complete it and your participation in the survey will end.

If you are ready to begin the survey at this time, please click Continue. If not, click Return Later and return to this site when it is convenient for you.

Please note: Do not use the browser's back button during this survey.

[END WELCOME PAGE]

[BEGIN ONLINE PREAMBLE 1]

Disclaimer

Thank you for your interest in this voluntary research survey about Humalog® KwikPen®, 200 units/mL (Humalog® U-200 KwikPen®), which is being conducted by United BioSource Corporation (UBC) on behalf of the sponsor, Eli Lilly and Company (Lilly), the marketing authorization holder of Humalog® U-200 KwikPen®. This survey is voluntary and you are under no obligation to participate. There are no known risks to you in taking this survey. You will not receive any direct medical benefit from taking part in the survey. You may refuse to take part or quit at any time without penalty or loss of benefits to which you are otherwise entitled. Your answers to the questions or your decision to take part in the survey will not affect your ability to receive or use Humalog® U-200 KwikPen®. Because this study is not designed to treat any illness or improve your health, your alternative is to not participate. There are no expected risks. Your response options may be removed from the survey for administrative reasons.

Before you begin, we would like to share some important information about this research survey. You are being asked to take part because you have filled or refilled a prescription for Humalog® U-200 KwikPen® in the past 90 days. The information collected in the survey you are about to take will help Lilly to know if patients understand important information about using the Humalog® U-200 KwikPen®. The survey will take about 15 minutes. If you are eligible to take the survey, complete all the questions, and provide your contact information, you will be compensated $20.00 in the form of a gift card.

How We Use Your Information

Your answers to the survey questions will be combined with those from other patients taking the survey, and none of the responses you provide will be able to be traced back to you. All answers will be put together and reported to Lilly, and the Food and Drug Administration (FDA).

Your name and address will only be used to send your compensation of $20.00 in the form of a gift card after you complete the survey. There is no cost to you for taking this survey.

How We Protect Your Privacy

We understand and respect that the privacy of your personal information is important to you. To the extent permitted by applicable laws and regulations, the records identifying you will not be made publicly available. All the information you provide will be kept strictly confidential. You will not be contacted for marketing purposes based on your personal information or your answers to the survey. Neither Lilly nor its contractors will sell, transfer, or rent your information. Your privacy will be

protected; however, research survey records may be inspected by the FDA and or a company called Sterling Institutional Review Board (the board which, in accordance with federal regulations, has reviewed this study). Your choice to provide Lilly with your information to is entirely voluntary but necessary to receive compensation. You do not waive any of your rights by taking part in this study.

How to Learn More about the Online Survey

The information in this survey should not take the place of talking with your doctor or healthcare professional. You do not waive any legal rights by taking part in this study. If you have any questions about your condition or treatment or that of the person you care for, or if you would like more information about Humalog® U-200 KwikPen®, talk to your doctor, pharmacist, or other healthcare professional.

If you have questions about or problems with the survey, please contact the Survey Coordinating Center at **1-844-810-8936**.

If you have questions regarding your rights as a research participant, or if you have questions, concerns, complaints about the research, would like information, or would like to offer input, you may contact the Sterling Institutional Review Board Regulatory Department, 6300 Powers Ferry Road, Suite 600-351, Atlanta, Georgia 30339 (mailing address) or at telephone number **1-888-636-1062** (toll free). Your IRB ID is 5523.

Taking the Survey

Once you have answered a question and moved on, you cannot go back and change your answers.

Thank you for your participation in this survey.

[END ONLINE PREAMBLE 1]

[BEGIN TELEPHONE PREAMBLE 1]

Disclaimer

Thank you for your interest in this voluntary research survey about Humalog® KwikPen®, 200 units/mL (Humalog® U-200 KwikPen®), which is being conducted by United BioSource Corporation (UBC) on behalf of the sponsor, Eli Lilly and Company (Lilly), the marketing authorization holder of Humalog® U-200 KwikPen®. This survey is voluntary and you are under no obligation to participate. There are no known risks to you in taking this survey. You will not receive any direct medical benefit from taking part in the survey. You may refuse to take part or quit at any time without penalty or loss of benefits to which you are otherwise entitled. Because this study is not designed to treat any illness or improve your health, your alternative is to not participate. There are no expected risks.

Before you begin, we would like to share some important information about this research survey. You are being asked to take part because you have filled or refilled a prescription for Humalog® U-200 KwikPen® within the past 90 days. The information collected in the survey you are about to take will help Lilly to know if patients understand important information about using the Humalog® U-200 KwikPen®. The survey will take about 15 minutes. If you are eligible to take the survey, complete all the questions, and provide your contact information, you will be compensated $20.00 in the form of a gift card.

How We Use Your Information

Your answers to the survey questions will be combined with those from other patients taking the survey, and none of the responses you provide will be able to be traced back to you. All answers will be put together and reported to Lilly, and the Food and Drug Administration (FDA).

Your name and address will only be used to send you $20.00 in the form of a gift card after you complete all the survey questions. There is no cost to you for taking this survey.

How We Protect Your Privacy

We understand and respect that the privacy of your personal information is important to you. To the extent permitted by applicable laws and regulations, the records identifying you will not be made publicly available. All the information you provide will be kept strictly confidential. You will not be contacted for marketing purposes based on your personal information or your answers to the survey. Neither Lilly nor its contracts will sell, transfer, or rent your information. Your privacy will be protected; however, research survey records may be inspected by the FDA and/or a company called Sterling Institutional Review Board (the board which, in accordance with federal regulations, has reviewed this study). Your choice to provide Lilly with your information to is entirely voluntary but necessary to receive compensation. You do not waive any of your rights by taking part in this study.

How to Learn More about the Survey

The information in this survey should not take the place of talking with your doctor or healthcare professional. You do not waive any legal rights by taking part in this study. If you have any questions about your condition or treatment or that of the person you care for, or if you would like more information about Humalog® U-200 KwikPen®, talk to your doctor, pharmacist, or other healthcare professional.

If you have questions about or problems with the survey, please contact the Survey Coordinating Center at **844-810-8936.**

If you have questions regarding your rights as a research participant, or if you have questions, concerns, complaints about the research, would like information, or would like to offer input, you may contact the Sterling Institutional Review Board Regulatory Department, 6300 Powers Ferry Road, Suite 600-351, Atlanta, Georgia 30339 (mailing address) or at telephone number **1-888-636-1062** (toll free). Your IRB ID is 5523.

Taking the Survey

Once you have answered a question and moved on, you cannot go back and change your answers.

Thank you for your participation in this survey.

[END TELEPHONE PREAMBLE 1]

[BEGIN SCREENING QUESTIONS]

Please provide a response to all questions and statements.

1. Do you agree to take part in this survey about Humalog® KwikPen®, 200 units/mL (Humalog® U-200 KwikPen®)?

   ○ Yes

   ○ No **[TERMINATE]**

[Q2 - FOR WAVE 2 ONLY]

2. Have you ever participated in this survey for Humalog® U-200 KwikPen® before?

   - ○ Yes **[TERMINATE]**
   - ○ No
   - ○ I don't know **[TERMINATE]**

3. Have you been diagnosed with diabetes?

   - ○ Yes
   - ○ No **[GO TO Q10, TERMINATE AFTER Q14]**
   - ○ I don't know **[GO TO Q10, TERMINATE AFTER Q14]**

4. How long have you had diabetes?

   - ○ Less than 1 year
   - ○ 1 – 5 years
   - ○ 6 – 10 years
   - ○ 11 – 15 years
   - ○ More than 15 years
   - ○ I don't know

5. Do you use injectable insulin to treat your diabetes?

- ○ Yes
- ○ No **[GO TO Q10, TERMINATE AFTER Q14]**
- ○ I don't know **[GO TO Q10, TERMINATE AFTER Q14]**
- ○ I don't have diabetes **[GO TO Q10, TERMINATE AFTER Q14]**

6. For how long have you been using injectable insulin to manage your diabetes?

- ○ Less than 1 year
- ○ 1 – 5 years
- ○ 6 – 10 years
- ○ 11 – 15 years
- ○ More than 15 years
- ○ I don't know **[GO TO Q10, TERMINATE AFTER Q14]**

7. Have you been prescribed Humalog® U-200 KwikPen® at least once?

- ○ Yes
- ○ No **[GO TO Q10, TERMINATE AFTER Q14]**
- ○ I don't know **[QO TO Q10, TERMINATE AFTER Q14]**
- ○ I don't have diabetes/I don't use insulin **[GO TO Q10, TERMINATE AFTER Q14]**

8. For how long have you been using Humalog® U-200 KwikPen®?

- ○ I have not used the Humalog® U-200 KwikPen® yet
- ○ Less than 3 months
- ○ 3 – 6 months
- ○ 7 – 12 months
- ○ More than 1 year
- ○ I don't know
- ○ I don't have diabetes/I don't use Humalog® U-200 KwikPen® **[GO TO Q10, TERMINATE AFTER Q14]**

9. What type of mealtime insulin did you use prior to using Humalog® U-200 KwikPen®?

- ○ Humalog® U-100 KwikPen®
- ○ Other 100 Units/mL insulin
- ○ I don't know
- ○ I don't have diabetes/I don't use Humalog® U-200 KwikPen® **[TERMINATE AFTER Q14]**

10. What is your gender?

- ○ Male
- ○ Female

11. What is the highest level of education you have completed?

- ○ Less than high school
- ○ Some high school
- ○ High school graduate/GED (General Education Diploma)
- ○ Some college/Associate's degree
- ○ Bachelor's degree
- ○ Master's degree
- ○ Professional or Doctoral degree
- ○ Prefer not to answer

12. In what state do you live?

[DROP-DOWN LIST INPUT WITH STATES TABLE, EXCLUDE PREFER NOT TO ANSWER]

13. Which of the following groups best describes your age?

- ○ Under 18 **[TERMINATE AFTER Q14]**
- ○ 18 – 29
- ○ 30 – 39
- ○ 40 – 49
- ○ 50 – 59
- ○ 60 – 69
- ○ 70 or older
- ○ Prefer not to answer **[TERMINATE AFTER Q14]**

14. Have you or any of your immediate family members ever worked for Eli Lilly and Company (Lilly), United BioSource Corporation (UBC), or the Food and Drug Administration (FDA)?

- ○ Yes **[TERMINATE]**
- ○ No
- ○ I don't know **[TERMINATE]**

[END SCREENING QUESTIONS]

[BEGIN SURVEY CONTENT]

[BEGIN PREAMBLE 2 – DISPLAY ON SAME PAGE AS NEXT QUESTION]

The following questions are about Humalog® U-200 KwikPen®.

[END PREAMBLE 2]

15. Please answer True, False, or I don't know for each of the following statements about Humalog® U-200 KwikPen®.

	[RANDOMIZE LIST]	**True**	**False**	**I don't know**
A	Humalog® U-200 KwikPen® should only be injected using the prefilled KwikPen device in which it is supplied.	○	○	○
B	Your dose of insulin does not need to be converted when changing from one strength of Humalog to the other (for example, changing from Humalog U-100 KwikPen to Humalog® U-200 KwikPen®).	○	○	○

16. Please answer Yes, No, or I don't know for each of the following statements about the Patient Information Letter/*IMPORTANT SAFETY INFORMATION FOR* Humalog® KwikPen®, 200 units/mL, U-200 *insulin lispro* injection.

	[RANDOMIZE LIST]	**Yes**	**No**	**I don't know**
A	The first time I was prescribed Humalog® U-200 KwikPen®, my doctor or nurse provided me with a paper copy of the Patient Information Letter/*IMPORTANT SAFETY INFORMATION*. *(This letter was included with the patient sample pen pack.)*	○	○	○
B	My doctor or nurse offered to explain information about the safe use of Humalog® U-200 KwikPen® the first time I was prescribed this product.	○	○	○
C	I think about the important safety information for Humalog® U-200 KwikPen® to remind myself of the risks when injecting my insulin.	○	○	○
D	I should always have a backup pen with me.	○	○	○
E	It is ok to transfer insulin from the pen using a syringe.	○	○	○

17. Other than the information you have received from your doctor or nurse, from what sources have you received and/or accessed information on the safe use and understanding of the Humalog® U-200 KwikPen®. (Please select all that apply.)

[RANDOMIZE LIST – KEEP OTHER AT THE BOTTOM]

☐ Pharmacist

☐ Other Healthcare Professional

☐ Diabetes Support Group

☐ Internet

☐ Product Warning Label

☐ Other

[TELEPHONE: BEGIN SAFETY EVENT/PRODUCT COMPLAINT – KEEP ON ONE PAGE]

(INTERVIEWER: Please record if respondent spontaneously reported a safety event or product complaint during the course of this interview.)

○ Yes

○ No **[GO TO CLOSING 1]**

Enter Safety Event or Product Complaint Verbatim

[MULTILINE INPUT]

(INTERVIEWER: Indicate to the respondent that someone may call back to ask more questions about the adverse event or product complaint that was reported.)

[END SAFETY EVENT/PRODUCT COMPLAINT]

[BEGIN CLOSING 1]

We would like to send you $20.00 as compensation for your time and effort as well as a copy of the Patient Communication for Humalog® U-200 KwikPen®, and the correct answers to key safety message questions , but we need your name and address to do so. Do you agree to provide your contact information for this purpose?

○ Yes

○ No **[GO TO CLOSING 2]**

[END CLOSING 1]

[BEGIN CONTACT INFORMATION]

FIRST NAME: **[FREE TEXT]**

LAST NAME: **[FREE TEXT]**

MIDDLE INITIAL: **[OPTIONAL; MUST BE 1- ALPHA CHARACTER]**

ADDRESS: **[MULTILINE INPUT]**

CITY: **[FREE TEXT]**

STATE: **[DROP-DOWN LIST INPUT WITH STATES TABLE]**

ZIP CODE: **[MUST BE 5-DIGIT NUMERIC-ONLY]**

[END CONTACT INFORMATION]

[BEGIN CLOSING 2]

This completes the survey. Thank you again for your participation.

[END CLOSING 2]

[END SURVEY CONTENT]

APPENDIX I.4 PATIENT SURVEY RECRUITMENT MATERIALS

[FOR REMINDER LETTER: "REMINDER" is stamped on the invitation letter and sent to non-respondents.]

CURR_DATE]

[PAT_FIRST_NAME] [PAT_LAST_NAME]

[PAT_STREET_ADDR]

[PAT_CITY], [PAT_STATE] [PAT_ZIP]

Dear [PATIENT FULL NAME]:

The purpose of this letter is to tell you about a voluntary survey being conducted by Eli Lilly and Company (Lilly), the maker of Humalog® U-200 KwikPen®, as part of an FDA (Food and Drug Administration) requirement to find out if patients understand important information related to taking Humalog® U-200 KwikPen®. Express Scripts and its subsidiary United BioSource Corporation (UBC) are looking for 280 people to complete this 15-minute survey on behalf of Lilly. Eligible individuals who complete the survey will be sent a $20 gift card to thank them for their time.

You may be eligible to participate if you have taken Humalog® U-200 KwikPen® and are 18 years of age or older. The survey asks various questions about the type of information you received about Humalog® U-200 KwikPen® and where you get your medical information.

If you are interested in participating and want to find out if you are eligible,

- Go to www.humalogsurveyus.com any time or
- Call **1-844-810-8936**, 8 a.m. to 8 p.m. Eastern Time, Monday through Friday

Please have this letter when you take the survey. You will be asked to give this code prior to starting the survey: [CODE_ID]

We recommend that you take the survey on a desktop or laptop computer. Taking the survey on mobile devices, such as smart phones, tablets, and e-notebooks, is not supported.

You are under no obligation to participate in this survey. If you choose to participate, please be assured that your contact information and your individual responses will be kept strictly confidential. However, if you wish to receive the $20 payment, you must provide us with your name and the mailing address of the place where you would like it delivered.

Your answers to the survey questions will be combined with answers given by others, and your name or other personal details you provide will not be used in any written report or publication. Neither taking the survey nor your answers to the questions will affect your ability to receive or take Humalog® U-200 KwikPen®.

Thank you in advance for your participation in this survey.

Sincerely,

Humalog® U-200 KwikPen® Survey Team

Express Scripts manages your prescription benefit from your employer or health plan.

This letter is intended for the addressee only and may contain information that is confidential or privileged.

[UBC LETTERHEAD]

[CURR_DATE]

[PAT_FIRST_NAME] [PAT_LAST_NAME]

[PAT_STREET_ADDR]

[PAT_CITY], [PAT_STATE] [PAT_ZIP]

Dear [PATIENT FULL NAME]:

On behalf of Eli Lilly and Company, the maker of Humalog® KwikPen®, 200 units/mL (Humalog® U-200 KwikPen®), we thank you for taking the time to complete the Humalog® U-200 KwikPen® Survey. To express our appreciation for your valuable time, enclosed is your $20 gift card for your time and effort.

Additionally, for your information and to reinforce the key safety messages about Humalog® U-200 KwikPen® we have also enclosed two documents:

1. A copy of the Patient Information Letter/IMPORTANT SAFETY INFORMATION. Humalog® KwikPen®, 200 units/mL, U-200 insulin lispro injection
2. The correct answers to the key safety messages for Humalog® U-200 KwikPen®.

Lastly, please read the enclosed Terms and Conditions document before using your gift card as well as the privacy policy that can be found at: http://www.ctpayer.com/downloads/privacy_policy.pdf

Sincerely,

The Humalog® U-200 KwikPen® Survey Team
1-844-810-8936
www.humalogsurveyus.com

Enclosed:

Gift Card, Terms and Conditions document and Frequently Asked Questions

Patient Information Letter/IMPORTANT SAFETY INFORMATION. Humalog® KwikPen®, 200 units/mL, U-200 insulin lispro injection

Correct Answers to Key Safety Messages

PATIENT CORRECT ANSWER DOCUMENT

Correct Responses to Select PATIENT Survey Questions about Key Safety Messages for Humalog© U-200 KwikPen©

Q: Please answer True, False, or I don't know for each of the following statements about Humalog© U-200 KwikPen©.

STATEMENT	Correct Response
Humalog® U-200 KwikPen® should only be injected using the prefilled KwikPen device in which it is supplied.	***TRUE***
Your dose of insulin does not need to be converted when changing from one strength of Humalog to the other (for example, changing from Humalog U-100 KwikPen to Humalog® U-200 KwikPen®).	***TRUE***

Q: Please answer Yes, No, or I don't know for each of the following statements about the Patient Information Letter/*IMPORTANT SAFETY INFORMATION* FOR Humalog© KwikPen©, 200 units/mL, U-200 insulin lispro injection.

STATEMENT	Correct Response
The first time I was prescribed Humalog® U-200 KwikPen®, my doctor or nurse provided me with a paper copy of the Patient Information Letter/*IMPORTANT SAFETY INFORMATION. This letter was included with the patient sample pen pack.*	***Yes***
My doctor or nurse offered to explain information about the safe use of Humalog® U-200 KwikPen® the first time I was prescribed this product.	***Yes***
I think about the important safety information for Humalog® U-200 KwikPen® to remind myself of the risks when injecting my insulin.	***Yes***
I should always have a backup pen with me.	***Yes***
It is ok to transfer insulin from the pen using a syringe.	***No***

If you have questions or are unclear about any of these responses, please refer to the Patient Communication on Important Safety Information for Humalog® U-200 KwikPen®.

PATIENT Surveyresponses_ Humalog® U-200 KwikPen® v1.0 13MAY2016 Page 1 of 1

APPENDIX I.5 DIRECT HEALTHCARE PROFESSIONAL COMMUNICATION ON THE CORRECT USE OF Humalog® KwikPen®, 200 units/mL

APPENDIX I.6 PATIENT COMMUNICATION: IMPORTANT SAFETY INFORMATION FOR HUMALOG® 200 UNITS/ML KWIKPEN® (INSULIN LISPRO)