LIONBRIDGE

SUCCESSFULLY AUTHORING AND TRANSLATING PLAIN LANGUAGE SUMMARIES

3 Mandates for Effective Communication

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In this paper, you'll learn:

Key aspects of the new regulation that impact the development of plain language summaries aligned with the new EU clinical trial regulation[1].

Three important points to bear in mind when developing a summation of the clinical research geared to a non-technical audience.

The value gained by partnering with a language service provider with dual expertise in linguistic sciences and life sciences, which can provide the know-how and global reach to infuse plain language literacy principles with accurate, compliant translation capabilities spanning all EU trial countries and beyond.

The Challenge of Change in Clinical Trial Results Reporting

We live in a world that places tremendous demands on the scientists who conduct and report on life-changing clinical research. No task exemplifies this truth better than the all-important Clinical Study Report, or CSR. The CSR is a key factual and objective report of the study's findings, which incorporates numerous data types spanning clinical and statistical descriptions, analyses and summations, tables and figures, and more.

Scientists tasked with drafting CSRs now face added pressure in the European Union (EU), where a pending regulation, (EU) No 536/2014, will require them to author a second report: a patient and public-friendly plain language summary of the trial results. The plain language summary is based on the information contained in the CSR and is due one year after the end of the trial.

Intended for lay persons[2], this summary must target specific audience profiles–from children to adults–across therapeutic areas, regions, and literacy levels. Scientists will subsequently need to ensure the plain language summary's accurate translation into the national language(s) of the countries where clinical trial participants were enrolled, in accordance with the strict timing and compliance requirements outlined in the regulation.

As a scientist, you're likely struggling with how to deliver on the expanded reporting requirements efficiently and accurately. You'll need to determine what skill sets to tap as your ongoing research responsibilities grow.

What's Needed: A Unique Combination of Skills

As a world-leading language service provider committed to compliance excellence, we understand your world—and the nuances of transforming scientific clinical research results into plain language. The multidisciplinary task of transforming highly technical scientific content into plain language terms demands a dual skill set of life science and linguistic science expertise. Competencies in both scientific domains are instrumental in engaging a plain language audience and ensuring full comprehension of your trial results.

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The Nuts and Bolts of the New Regulation

Though plain language summaries are not new to clinical investigations, they have recently gained traction in life sciences due in part to a public push for transparency and ethical disclosure of research results generated in the medical community. The EU's upcoming Clinical Trial regulation makes mandatory the provision of plain language summaries by all sponsors in the European Union conducting:

- Interventional (including low-interventional) clinical trials
- Phase 1 to Phase 4 trials that take place in at least one site in the EU region

Note: Plain language summaries are not required for studies investigating devices or diagnostic products at this time.

Under the new regulation, the European Commission will establish a publicly-accessible EU database to ensure a sufficient level of transparency within clinical research and grant the public access to relevant information on clinical trials, including plain language summaries of clinical trial results. This legal enforcement now requires clinical trial sponsors to develop standard internal processes and to dedicate resources to clinical trial disclosure activities.

General consensus suggests that disclosing research results to public audiences in plain language is necessary for three important reasons:

To increase health literacy of the general population

To increase public willingness to participate in and engage with clinical trials

To spur the development of new research strategies

Additionally, patients can be valuable sources of information to researchers striving to understand the effects of a disease on a patient's life, design protocol procedures, or ensure the readability and usability of labeling and product information. Communicating to a global patient population through a plain language summary broadens a researcher's ability to gain important insights and allows more patients to benefit from the research.

While the EU has taken an early lead in regulating the disclosure of clinical research results in plain language, other countries and regions are expected to follow suit.

Communicating a Science Story to the General Public: 3 Mandates to Bear in Mind

Scientists and medical writers are trained to publish scientific papers and communicate with peers who share their knowledge, prerequisites, terminology, and communication style. These clinical experts, entrenched within a homogeneous medical academic community that champions shared specialized knowledge, may find it difficult to relate to public perception of their work[3]. That makes adapting highly technical communications to a plain language audience—and thus complying with the new EU regulation—a challenge.

A scientist tasked with communicating effectively with the public must meet three mandates:

1. **Understand the target audience** by analyzing how a broad, heterogeneous public audience with no presumed knowledge of clinical research or medical terminology can parse scientific content intended for a specialized medical community

2. **Communicate to the appropriate literacy level** by ensuring content is adapted to the literacy level of the general population and the clinical trial population in accordance with principles of health literacy and numeracy

3. **Translate summaries into unambiguous local language** by using the power of linguistics to produce high-quality translations of master plain language summaries without sacrificing meaning, scientific validity, or consistency of the source content, or unintentionally using promotional or biased language

LET'S EXPLORE EACH ONE.

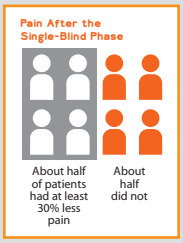
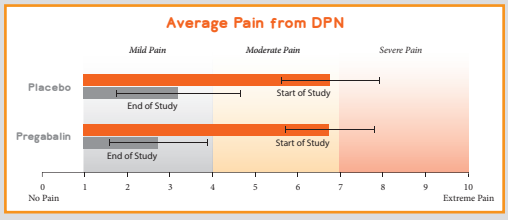
1 Understand the Target Audience

As with any other communication, authoring a successful plain language summary begins by analyzing and understanding your target audience. A trial sponsor may find it appropriate to develop separate summary templates for:

- Clinical trials in adults and children
- Distinct geographic territories
- Specific therapeutic areas

Analyzing the particular audience informs your communication approach and helps strike the right balance between written and visual content. A summary intended for children or adolescents, for example, or a trial that has recruited patients in third-world countries with below average literacy levels, might reasonably include more infographics, cartoons, or other visual descriptions, designs, and/or representations to convey results most effectively to the target audience.

Below are examples of the different language styles used in scientific and plain language content[4].

SCIENTIFIC LANGUAGE	PLAIN LANGUAGE
Full clinical protocol title "A 24-week treatment, multicenter, randomized, double blinded, double dummy, parallel-group, clinical trial evaluating the efficacy and safety of aclidinium bromide 400 µg/formoterol fumarate 12 µg fixed-dose combination BID compared with each monotherapy (aclidinium bromide 400 µg BID and formoterol fumarate 12 µg BID) and tiotropium 18 µg QD when administered to participants with stable chronic obstructive pulmonary disease."	**Short study title in the plain language summary** "A study to learn how 2 drugs taken together affects participants with COPD compared to taking them separately, and if they are safe to take together."
Results from scientific publication "Pregabalin numerically improved all measures assessed during the single-blind phase. At the end of the double-blind withdrawal phase, there was no significant difference in the primary endpoint of mean pain score (LOCF) between pregabalin and placebo (least squares mean difference, -0.32), although there was a significant difference in the BOCF analysis (least squares mean difference, -0.51). Pregabalin was associated with a significantly longer time to loss of pain response versus placebo during double-blind treatment, and some aspects of sleep and QOL also showed significant improvements with pregabalin."	**Results from plain language summary** No pregabalin did not relieve the pain of DPN any better than the placebo, which contained no medicine. Let's take a closer look at the study results to see what happened in each phase of the study. **Single-Blind Phase** - In this part of the study, 665 patients took pregabalin for up to six weeks. At the end, about half of the patients had at least 30% less pain and could move on to the double-blind phase, and half did not. **Double-Blind Phase** - There were 294 patients in this part of the study: 147 patients took pregabalin, and 147 took the placebo. Two more patients were assigned to the placebo group, but decided to leave the study before treatment started. The chart below compares how much pain both groups of patients had at the start and end of the study.   All patients started the study with a similar amount of pain, on average. At the end of the study, patients who took pregabalin in the double-blind phase had about the same amount of pain as patients who took placebo in the double blind phase, on average. This means that pregabalin did not work better than the placebo, which had no medicine in it.

Adverse events from scientific summary report Safety Results

- 127 AEs were reported for 17 subjects (94.4%) in the LEO 32731 group and 57 AEs were reported for 16 subjects (88.9%) in the placebo group. 106 of the AEs reported in the LEO 32731 group and 28 of the AEs reported in the placebo group were assessed as possibly or probably related to the treatment.

- The most common AEs in the LEO 32731 group were within the SOC gastrointestinal disorders, in particular nausea and diarrhea, most of which were considered treatment-related

- Most AEs were mild or moderate. 1 subject in the LEO 32731 group had 1 severe AE (increased alanine aminotransferase, considered possibly related to the IMP). 2 subjects in the placebo group had a total of 3 severe AEs (toothache, abdominal pain, and abdominal cramps).

- No subjects died during the trial. 3 serious AEs (SAEs) were reported: 2 subjects in the LEO 32731 group had 1 SAE each (ureterolithiasis, considered not related to the IMP, and erysipelas on the arm, considered possibly related to the IMP) and 1 subject in the placebo group had 1 SAE ('condition aggravated', relating to pre-existing Scheuermann's disease and considered not related to the IMP).

- AEs leading to withdrawal from the trial were reported for 9 subjects (50.0%) in the LEO 32731 group and 3 subjects (16.7%) in the placebo group. In the LEO 32731 group, the majority of AEs leading to withdrawal were within the SOC *gastrointestinal disorders*.

- ECG monitoring and evaluations of vital signs and clinical laboratory parameters showed no findings of concern.

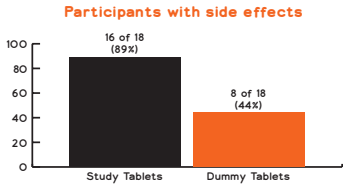
Adverse events in plain language summary

8. What were the side effects?

The graph and text below show the side effects that the study doctors believed were caused by the treatments.

24 of the 36 participants (67%) in this study had side effects.

More participants who took the study tablets had side effects compared with those who took dummy tablets.



Serious side effects
1 participant had a side effect that was rated as serious because the participant had to go to the hospital.

The participant took the study tablets. The side effect was a skin infection on the arm. The study doctor thought the infection might have been caused either by the study tablets or by the participant scratching or picking at the skin. The participant was treated with antibiotics at the hospital, and the infection cleared up. Afterwards, the participant continued in the study.

Most common side effects
The most common side effects were *gastrointestinal*, which means related to the stomach or gut. Examples are nausea (feeling sick or queasy), vomiting, stomach ache, and diarrhoea.

More participants who took the study tablets had gastrointestinal side effects compared with those who took dummy tablets:

- 16 of the 18 participants who took study tablets had 52 cases of gastointestinal side effects.

- 4 of the 18 participants who took dummy tablets had 8 cases of gastrointestinal side effects.

What does this mean for you? You'll need to consider:

Scope—is all the plain language summary information required by the Regulation available?

Organization—how should you compile the summary to generate maximum clarity?

Visuals—what is the ideal balance of words and images, and what graphic style should you use when creating images?

Comprehension—how can you transform your content so it is best understood by your target audience?

As a scientist, it's your task to communicate effectively with those who don't have your level of expertise. You'll need help constructing audience-centered communication that prioritizes literacy, readability, and language when adapting your clinical content to the plain language audience.

Want to learn more about the study of meaning derived from words? Download bonus content here.

As these examples illustrate, disclosing scientific research results to a public audience is more than an exercise of repackaging medical terminology in simple language. It is fundamentally about communication—that all-important "process where information is exchanged between audiences through a common system of symbols, signs or behavior.[5]" Transferring scientific language to plain language takes more than common sense and extra time: it requires an intimate understanding of the way specific humans use language and images to communicate.

When human beings communicate, we use words that can be described as symbols or signs. Words are different from other symbols, such as the icons used on a drug product label, because the relationship between the word and the entity it symbolizes is much more complex[6]. We derive meaning from a given word based on our experiences, educational level, and the context in which that word appears. For example, the word pain in English is defined as "bodily suffering or distress, as due to injury, illness, etc.[7]" Most of us regard pain as a temporary unpleasant condition. On the other hand, a patient with chronic pain symptoms may perceive pain as a permanent inconvenience and associate pain with loss of quality of life, despair, or insomnia. The word itself thus takes on a vastly different meaning for the average person and the chronic pain sufferer.

2 Communicate to the Appropriate Literacy Level

The guidelines released in the EU and US in 2017 and 2018 build on principles of health literacy and numeracy.[8] The European Health Literacy Consortium defines health literacy as being "linked to literacy and entails people's knowledge, motivation and competences to access, understand, appraise, and apply health information in order to make judgments and take decisions in every-day life concerning health care, disease prevention and health promotion to maintain or improve quality of life during the life course.[9]" Numeracy, as defined by the UK's National Numeracy Organization, is "the ability to use mathematics in everyday life.[10]"

Health literacy presumes a public audience with a low to average level of general literacy. In Europe, that is equivalent to a proficiency level of 2-3 according to The International Adult Literacy Survey (IALS), which has identified five proficiency levels.[11] A 2-3 proficiency level means that an individual can identify words and numbers in a context and can respond with simple information. Level 3 corresponds to high/secondary school completion levels, where the individual is able to understand, synthesize, and respond to information. A person at the lowest level (level 1) is capable of basic identification of words and numbers, and at the highest level (level 5) the person can demonstrate sophisticated skills in handling information.

The guideline provides templates that are intended to help clinical trial sponsors produce consistent plain language summaries that will help the public and patients improve familiarity and understanding of clinical research. Plain language summaries written for a public audience should use simple everyday language equivalent to a proficiency level of 2-3, or a sixth to eighth grade reading level in the US.

But effective communication transcends merely identifying the appropriate literacy level and adapting content to meet it. Scientists drafting plain language summaries need to keep a myriad of guideline[12] "dos" and "don'ts" in mind:

DO	DO NOT
Ensure content and layout are adapted to the general public regarding language, style, and literacy level. Use "white space" visual aids, or graphics insofar as they enhance communication for the target audience	Presume the target audience has any knowledge of the clinical study, of medical terminology, or of clinical research in general
Present information in a factual and neutral manner (e.g. "people who took drug A had fewer episodes of low blood sugar (hypoglycemia) than people who took drug B")	Use promotional or unduly positive language that can be perceived as marketing communication (e.g. "drug A works better than drug B")
Use simple words and unambigous everyday language (e.g. "high blood pressure" instead of "hypertension" and "use" instead of "utilize"	Use complex medical or technical terms unless explained in simple language or scientific jargon that can be misunderstood or mislead the reader (e.g. "significant" or "acute")
Present numerical information in absolute, whole numbers without decimals or as a percentage	Present numerical information as odds ratios or relative risks
Use short simple sentences and few sub-ordinate/dependent clauses	Use multisyllabic words (such as "unanticipated") or multiple sub-ordinate clauses
Use active voice where the subject of the sentence performs the action (e.g. "the researchers studied the effect of the drug on diabetes")	Use passive voice where the subject receives the action (e.g. "the effect of the drug on diabetes was studies by researchers")
Use respectful and empowering language to avoid victimising the clinical trial participants (e.g. "Patients living with dementia")	Victimize the patient by using terms such as "sufferers" or "demented"

A Word on Readability

The EU guideline recommends that clinical trial sponsors use language-specific reading tests to verify their plain language summaries are in fact readable. Below are some considerations when confirming the summary's readability.

Software Tools:

- Check readability via a MS Word software tool using the Flesch Reading Ease test or the Flesch-Kincaid Grade Level test, which are both based on counting syllables and sentence length.
- The Flesch-Kincaid Grade Level test translates scores to the US school grading system. The ideal reading level is 6th grade, equivalent to the average literacy level of the public.
- While software tools can indicate the optimal reading level, they do not consider the language conventions of a target audience. When human beings communicate, we use agreed-upon conventions to interpret words and text. These conventions can be specific to a profession, a culture, a lifestyle, or a life situation. In essence, communication could not take place without them. Given this limitation, the summary may not be readily understandable by the reader, even if the text is written at the correct reading level.
- Software readability tools are also limited in their ability to allow the reader to assess visuals or ascertain whether study participants will find the tone of voice in the summary to be respectful and empowering.

Pilot Testing:

- You can also verify readability by engaging a group of people or patients who represent the target audience.
- From a linguistic perspective, you can most effectively test readability directly with the target audience to capture the connotations the reader will derive from the content.

Outside Testing Expertise:

- To ensure you are receiving the most objective feedback on how you are presenting your clinical trial results, you could engage an independent editor to review the summaries.
- An independent service provider offers unbiased linguistic expertise to safeguard against the incorporation of any promotional content.

While trial sponsors must always strive to balance quality and costs, testing the master plain language summary with the target audience is recommended from both a linguistic and communications perspective. Smart firms will find a trusted partner that can provide invaluable linguistic and editorial insight at the ideal point in the development process—and in a turnkey fashion.

3 Translate Summaries Into Local Country Language

Throughout the communication process, authors should not only be attentive to the target audience and its literacy levels—they should also understand that expertise in linguistics is required to truly resonate with a plain language population in their local language.

Linguistics forms the foundation of a well-translated document. What is it? Linguistics is the scientific study of language, which explores humans' ability to communicate through language. Linguists determine how a person's use of language interacts with other cognitive processes when acquiring knowledge, such as the processes of evaluating and generating meaning.[13]

As illustrated below, the linguistic differences between scientific and plain language content are significant.

Linguistic traits of scientific research content:

- Complex syntactical sentence structures
- Technical terminology
- Complex words
- Professional jargon
- Passive language
- Impersonal tone of voice

Linguistic traits of lay language content:

- Simple syntactical sentence structures
- Straightforward language
- Simple words
- Common terms
- Active language
- Engaging tone of voice

Without proper linguistic expertise or training in the nuances of communicating to plain language audiences, the work involved in translating falls short. Authoring the plain language summary in its source language based on health literacy principles often ensures the original document's strength. Working with an experienced language service provider with linguistics expertise assures the author that translated versions will deliver that same level of understanding to the reader.

Once authoring is complete in the source language, the new regulation requires the summary to be translated into the national languages of the countries in which clinical trial participants were enrolled. Often, clinical trial sponsors will translate summaries for all countries where volunteers were recruited. Typically, the master plain language summary is authored in English based on a final (or close-to-final) CSR, then translated into the languages consistent with the translation of the Informed Consent.

Given that a phase 3 trial may enroll volunteers in multiple countries, clinical trial sponsors are advised to implement a standard translation process, which preferably centralizes translations to ensure consistency. By controlling the translation process and the templates translators use, trial sponsors can ensure they maintain high quality and integrity standards. What's more, a centralized process helps achieve equivalence in meaning and style between all translated versions and the master summary. Glossaries and translation memories are key tools in obtaining consistency in terminology and staying true to the source text.

In their desire to control the translation process, many trial sponsors involve in-country reviewers–most often affiliate employees. In-country reviewers, however, are not necessarily trained in plain language communication, linguistics, or health literacy—and thus cannot ensure their translations will deliver adequate resonance to the target audience or adhere to the master summary.

> **A well-honed life science skill set combined with linguistics expertise ensures the relevance and understanding of the plain language summary's adapted content.**

This Regulation is New. The Skill Set is Not.

Transferring a research summary into plain language is a multidisciplinary task that requires a combined skill set of life science and linguistic expertise. Where life science delves into the science of living organisms—their life processes, structure, and behavior—linguistic science examines how language is stored in the human brain, how we process meaning, and how we use language as a part of everyday life. Understanding how humans process meaning is essential in understanding the communication challenges plain language research summaries present.

Pairing life science with linguistic experience for plain language summary development offers three advantages:

1. Accurate reconstruction of scientific nomenclature into patient-friendly terminology
2. Predictive reliability in language effectiveness
3. Understandable science-minded communication tailored and translated across audiences, cultures, and geographies

If you're grappling with how your organization will tackle this new regulation, you're not alone. Although plain language summaries for trial participants are not new for many trial sponsors, this is a new regulatory requirement for everyone involved, from study sponsors to regulators to the general public and to language service providers.

But the required skill set is not new. At Lionbridge, we have spent 20 years perfecting the linguistic mechanisms involved in clinical translation. Our well-honed clinical expertise serves as the backbone to satisfying the multidisciplinary requirements of plain language summaries.

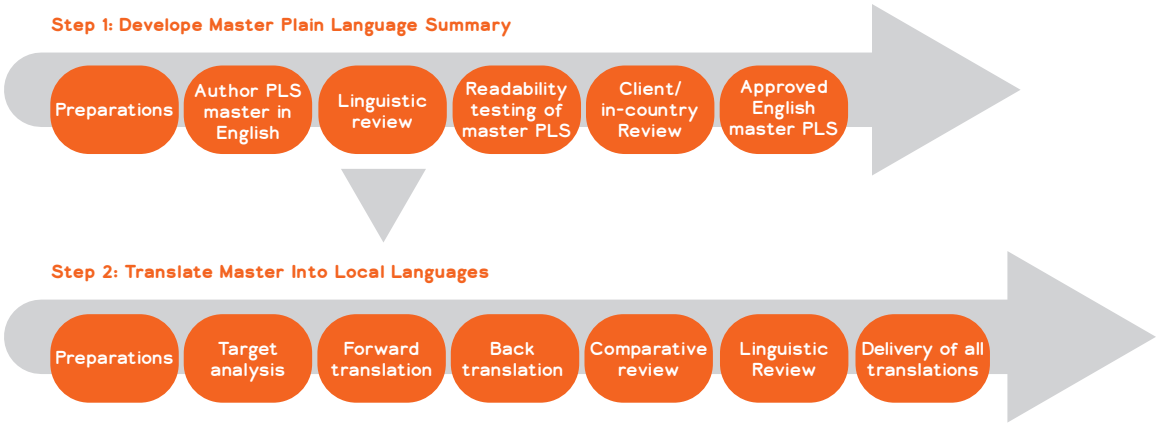
Consider this: clinical trial participants regularly interact with the trial's site staff throughout the enrollment, treatment, and follow-up phases of the trial. The documents used during these interactions—informed consent forms, patient information sheets, patient diaries, visit schedules, patient-reported-outcome questionnaires, etc.—require the deft intertwining of scientific and plain language.

Much like these essential patient-facing trial documents, which we have developed and translated with plain language in mind, plain language summaries need to effectively capture and communicate the final word to patients regarding the trial's outcomes.

Support Success by Using a Streamlined Process

The European Union has 24 official languages,[14] and that scope necessitates the enactment of a comprehensive process for plain language summary adaptation and translation. We have developed a best practices model and templates constructed for compliance for the development of a master plain language summary and subsequent translations that fully satisfy all requirements of the EU regulation.

We make it easy for you with a streamlined workflow:



A Trusted Partner that Keeps You Informed

As the new regulation progresses to enforcement, we'll help you satisfy your content and language requirements with confidence. Whether you are a scientist, medical writer, or clinical trial disclosure specialist, we're ready to serve as your partner for plain language summaries and help you gain the cost efficiencies and integrated expertise you seek. You can work with our clinical experts and project managers across the translation continuum or select the specific set of services that complement your internal capabilities. Our top priority is to help our life sciences customers succeed as the regulations are implemented and the scope of communication to a broader set of audiences with differing content requirements expands.

And as more supporting tools emerge, such as the recent recommendations from the MRCT and the European Commission's EU expert group, we can help you make sense of them all. We maintain a pulse on the regulatory industry by attending key conferences and keeping abreast of all current updates related to the new regulation. **We are excited to turn what could be considered a daunting challenge into an unexpected opportunity.**

Let Us Help

Contact us today to talk with an expert and learn how plain language summary authoring and translation with Lionbridge can improve the understanding and impact of your EU clinical trials and beyond.

Get started.

Footnotes

1. Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC.
2. Lay person as defined in the EU regulations, EU 2017/745, 5 April 2017; "an individual who does not have formal education in a relevant field of healthcare or medical discipline".
3. Radford T.; Of course scientists can communicate. Nature 2011; 469:445
4. All the examples are presented exactly "as is" and have been made publicly available by the trial sponsor. Lionbridge has no purpose of using the text in this context other than for exemplification.
5. Meriam-Webster.com
6. Describing Language, David Graddol et. al. Open University Press, 1994.
7. Webster's Encyclopedic Unabridged Dictionary of the English Language; dilithium Press Ltd.; 1989
8. "Summaries of Clinical Trial Results for Laypersons, Recommendations of the expert group on clinical trials for the implementation of Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use; Version 2; 5 February 2018" & "MRCT Center Return of Aggregate Results to Participants; Guidance Document, Version 3.1, 22. Nov. 2017".
9. WHO Health literacy, The solid facts, 2013; Ilona Kickbusch, et al.
10. https://www.nationalnumeracy.org.uk/what-numeracy
11. International Adult Literacy Survey (IALS), National Center for Education Statistics; https://nces.ed.gov/surveys/ials/proficiency.asp
12. https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/2017_01_26_summaries_of_ct_results_for_laypersons.pdf
13. www.linguisticsociety.org, The Science of Linguistics
14. www.Ethnologue.com

About Lionbridge

Lionbridge partners with brands to break barriers and build bridges all over the world. For more than 20 years, we have helped companies connect with global customers by delivering marketing, testing and globalization services in more than 300 languages.

Through our world-class platform, we orchestrate a network of 500,000 passionate experts in 5,000-plus cities, who partner with brands to create culturally rich experiences. Relentless in our love of linguistics, we use the best of human and machine intelligence to forge understanding that resonates with our customers' customers. Based in Waltham, Mass., Lionbridge maintains solution centers in 27 countries.

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