Collaboration With Multiple State Cancer Registries for a Data Linkage Drug Safety Surveillance Study – Yes You Can!

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ABSTRACT

Background: The Forteo Patient Registry is a voluntary prospective cohort study designed to estimate the incidence of osteosarcoma in patients taking teriparatide. Adult patients residing in the United States who provide consent will be enrolled over 5 years. Data are linked with participating state cancer registries for 12 years to ascertain cases diagnosed after patients started treatment.

Objective: To describe the recruitment of state cancer registries into this safety surveillance study and the progress with the first annual data linkage.

Methods: Cancer registries in all 50 states and the District of Columbia were invited in May 2009 to participate in the first annual linkage. A database was developed to track the recruitment process. All necessary applications and agreements for study approval were submitted to cancer registries. Registries that completed all local approval requirements and attended training on a standard linkage algorithm were included in the first annual linkage in September 2010.

Results: In total, 42 cancer registries, having 78 unique reviews (IRB or other), expressed an interest in participating and 27 (covering 70% of the adult US population) participated in the first annual data linkage. Of those 42 registries, 28 required local IRB review and 14 accepted the RTI IRB review. At least one additional approval was required at 36 of the 42 registries. For the 27 states participating in the first linkage, the average time from submission of the first application to the date a registry was linkage-ready was 94 days (range: 10 days to 195 days). The remaining registries are in the process of obtaining future approval.

Conclusions: Although there are substantial challenges to conducting a linkage study involving many state cancer registries, the results of the first linkage indicate that it is feasible for a large number of states to perform a data linkage concurrently using a standard data-linkage algorithm.

INTRODUCTION

- Teriparatide (Forteo) was initially approved in 2002 in the United States (US) for treatment of postmenopausal women with osteoporosis and for men with low bone mineral density at high risk for bone fractures.
- In rat toxicology studies, teriparatide caused increases in bone mass and a dose-dependent increase in the incidence of osteosarcoma.[1]
- In July 2009, as a condition of approval of a new indication for Forteo, the FDA required the implementation of a voluntary, prospective registry to estimate the incidence of osteosarcoma in patients receiving treatment with Forteo. A prospective study of Forteo users and linkage with cancer registries was designed for the following reasons:
  - Despite the availability of large health care databases for studies of acute adverse effects of medications, no existing source exists for capturing rare events.
  - Cancer registries offer a primary source for comprehensive and accurate capture of all cases of tumors such as osteosarcoma.
- Adult patients (aged 18 years and older) are invited to participate in the registry through a variety of methods. Participation involves providing signed consent and a small amount of data at the time of enrollment. No further contact is made with the participants.
- The study requires a large sample size of Forteo users from across the US and participation by a large percentage of US cancer registries, because adult osteosarcoma is rare (2.7 cases per million persons per year). The goal for the first year was to link with a minimum of 25 state cancer registries.
- In order to achieve the goal for state cancer registry participation, a structured registry recruitment plan, linkage algorithm, and training program were put in place.
- The study has been approved by the RTI Institutional Review Board (IRB), which serves as the primary IRB for the Forteo Patient Registry and as the central IRB for state cancer registries that can defer to a central IRB.

AIM

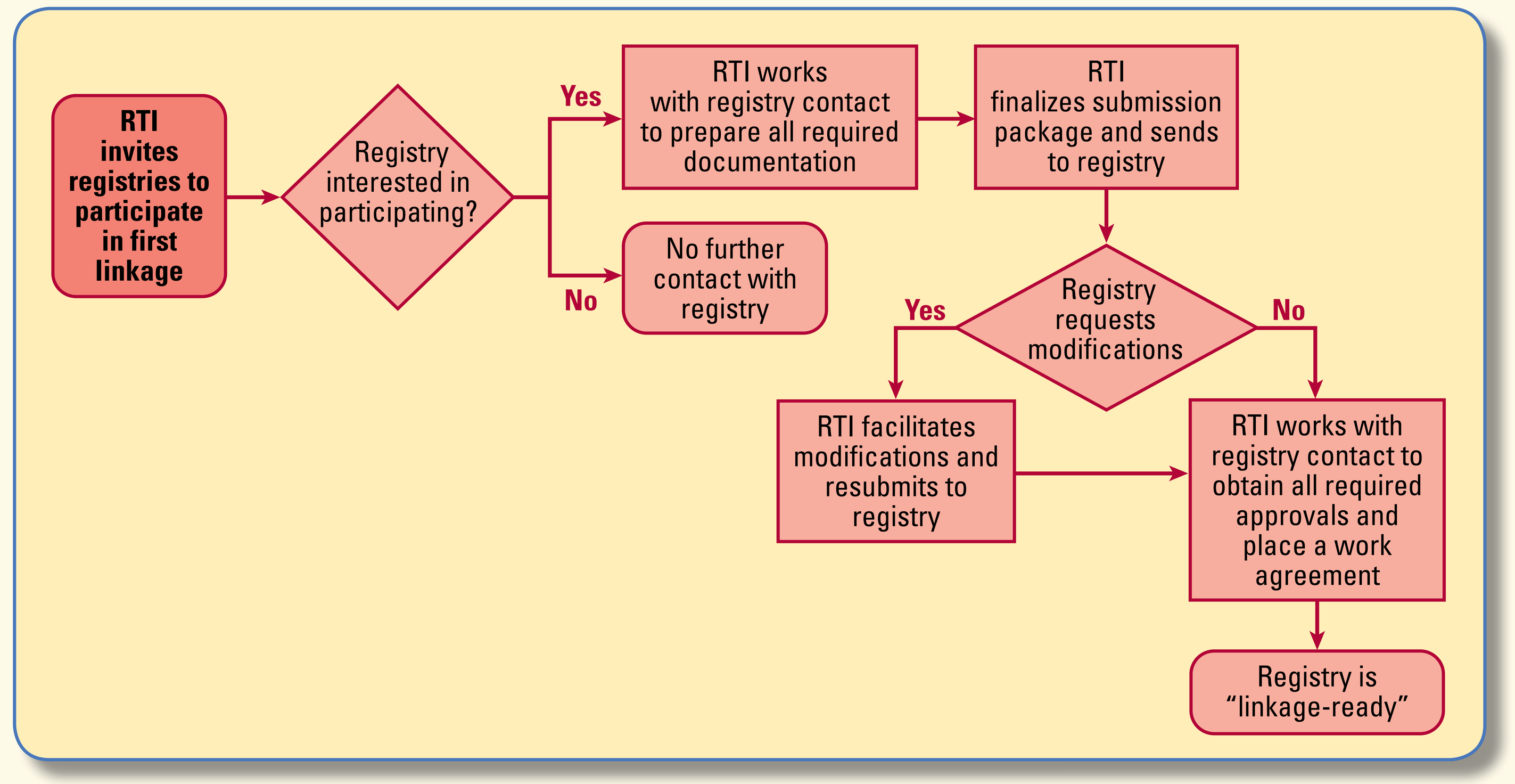
- The aim for this poster is to describe the results of the structured approach for registry recruitment and the first linkage of this safety surveillance study.

METHODS

Registry Recruitment

- Cancer registries in all 50 states and the District of Columbia were invited to participate by RTI in May 2009.
- States that expressed interest were contacted, and their specific requirements for study approval were assessed.
- The recruitment process was tracked using a database designed for this purpose.
- RTI developed standardized text for responses anticipated by the IRB and privacy requirements for use in the application process for individual registries.
- All necessary applications and agreements for study approval, including ethics and data use agreements, were submitted to individual state cancer registries.
- States were considered "linkage-ready" once all required approvals were obtained and a work agreement was established.
- Figure 1 shows the planned approach to cancer registry recruitment.

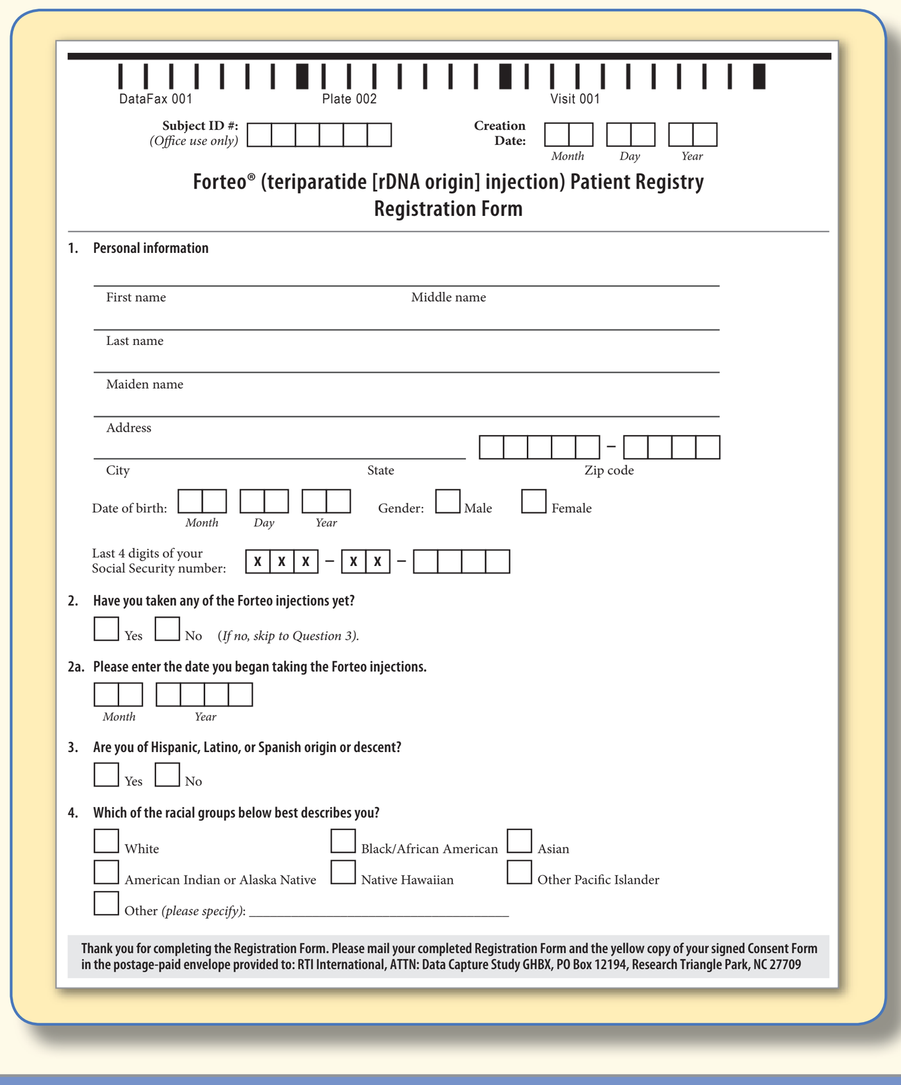
Figure 1. Registry Recruitment Plan



Linkage

- Cancer registries were trained to use a standard linkage algorithm created and tested by RTI International[2] in collaboration with three registries that reviewed the algorithm and procedures.
- Link Plus (v2.0), a probabilistic matching software program available from the Centers for Disease Control and Prevention, was used to develop the algorithm.
- Link Plus was selected because it was designed specifically for linking with state cancer registry data, is easy to use, and is readily accessible.
- Registration data (Figure 2) from eligible patients enrolled in the study as of July 26, 2010, were sent to participating state cancer registries via a secure FTP.
- Registries used a standardized form to document results of the linkage, including the number of osteosarcoma cases in their database and whether any matched with the Forteo registry participants provided by RTI.

Figure 2. Forteo Patient Registry Registration Data



DataFax 001 Plate 002 Visit 001

Subject ID #: (Office use only) Creation Date: Month Day Year

Forteo® (teriparatide [rDNA origin] injection) Patient Registry Registration Form

1. **Personal information**

   First name Middle name

   Last name

   Maiden name

   Address

   City State Zip code

   Date of birth: Month Day Year Gender: Male Female

   Last 4 digits of your Social Security number: X X X – X X –

2. **Have you taken any of the Forteo injections yet?**

   Yes No *(If no, skip to Question 3).*

2a. **Please enter the date you began taking the Forteo injections.**

   Month Year

3. **Are you of Hispanic, Latino, or Spanish origin or descent?**

   Yes No

4. **Which of the racial groups below best describes you?**

   White Black/African American Asian

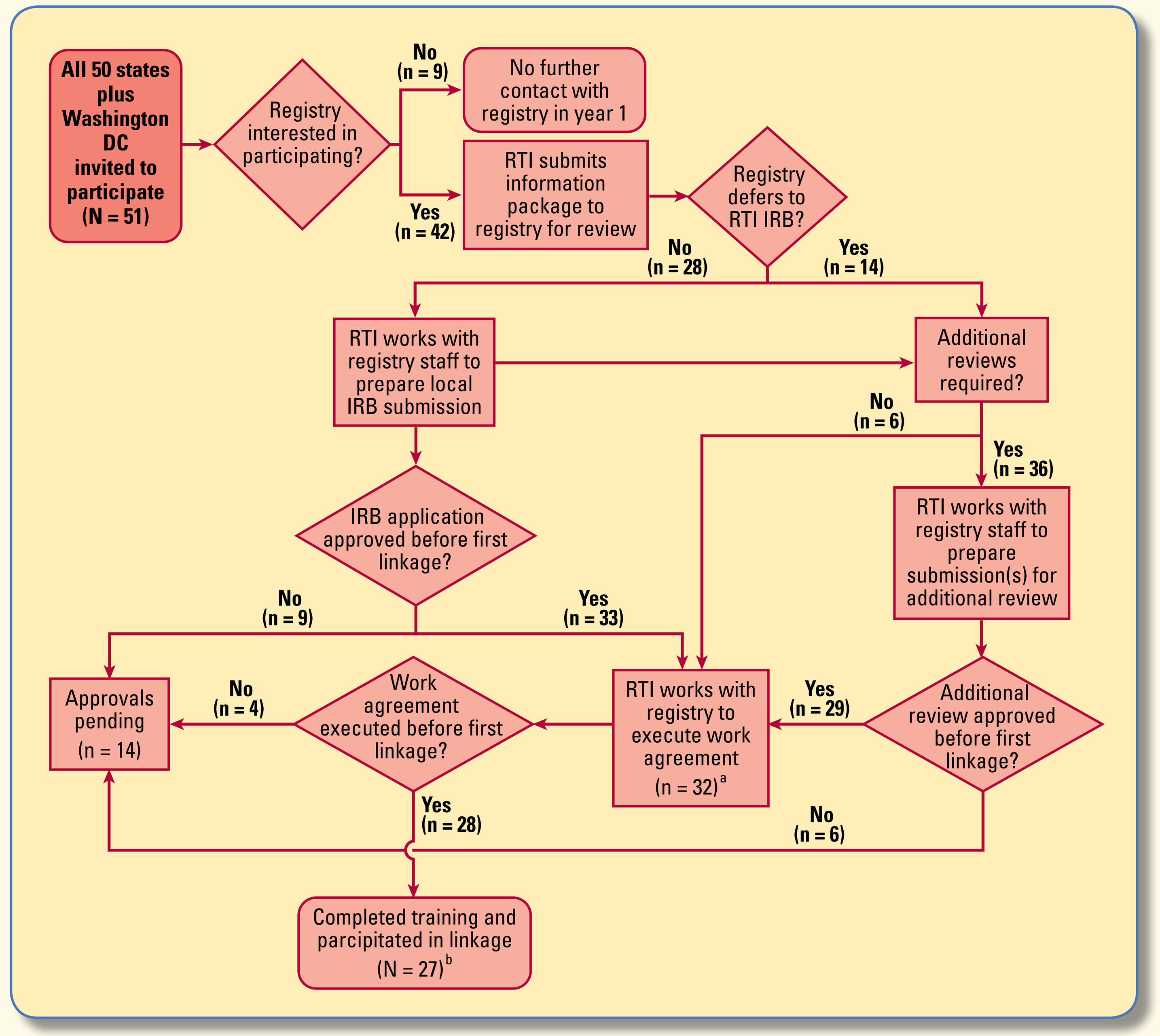
   American Indian or Alaska Native Native Hawaiian Other Pacific Islander

   Other *(please specify)*:

Thank you for completing the Registration Form. Please mail your completed Registration Form and the yellow copy of your signed Consent Form in the postage-paid envelope provided to: RTI International, ATTN: Data Capture Study GHBX, PO Box 12194, Research Triangle Park, NC 27709

RESULTS

Figure 3. RTI Composite Experience for Registry Recruitment



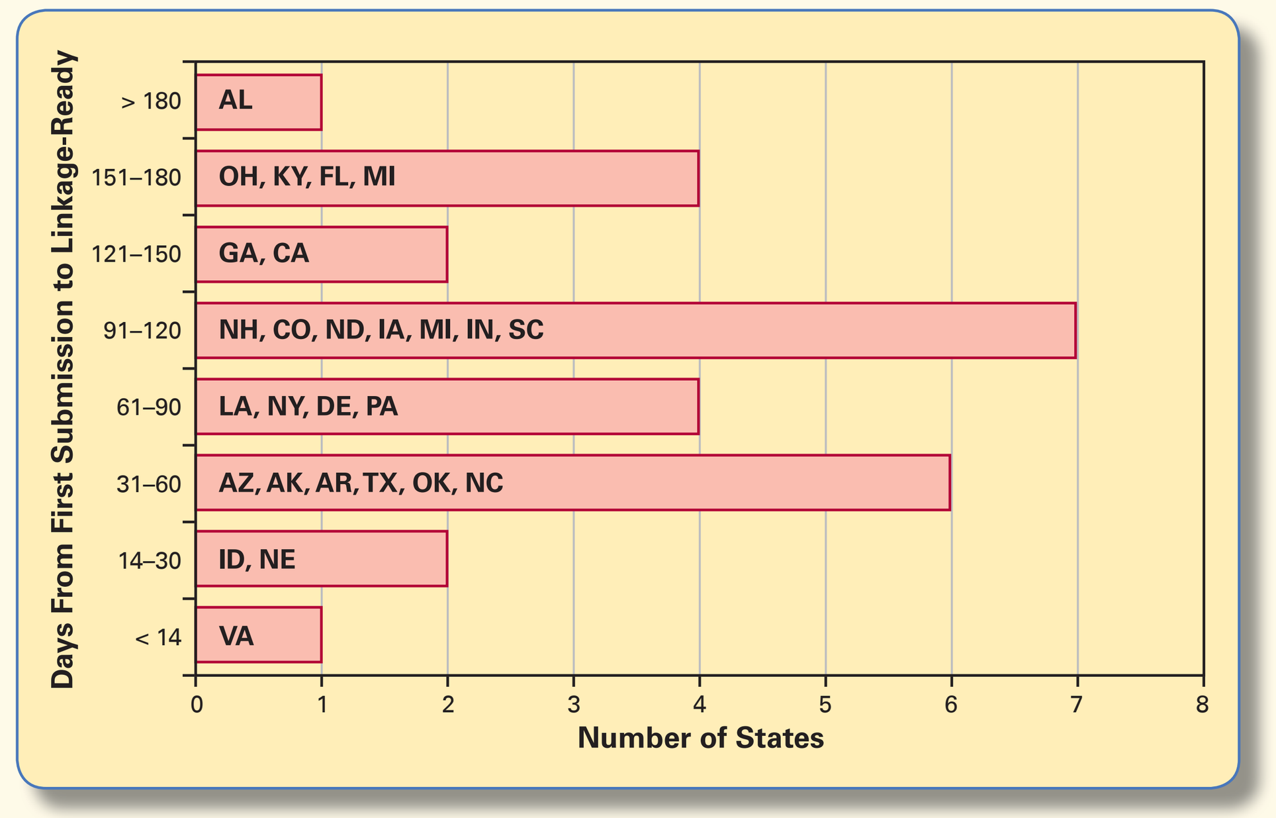
a IRB approval and additional review approved are not mutually exclusive; therefore, number moving to work agreement is less then sum of those two boxes.

b One registry was not able to participate in the linkage due to resource constraints.

Registry Recruitment

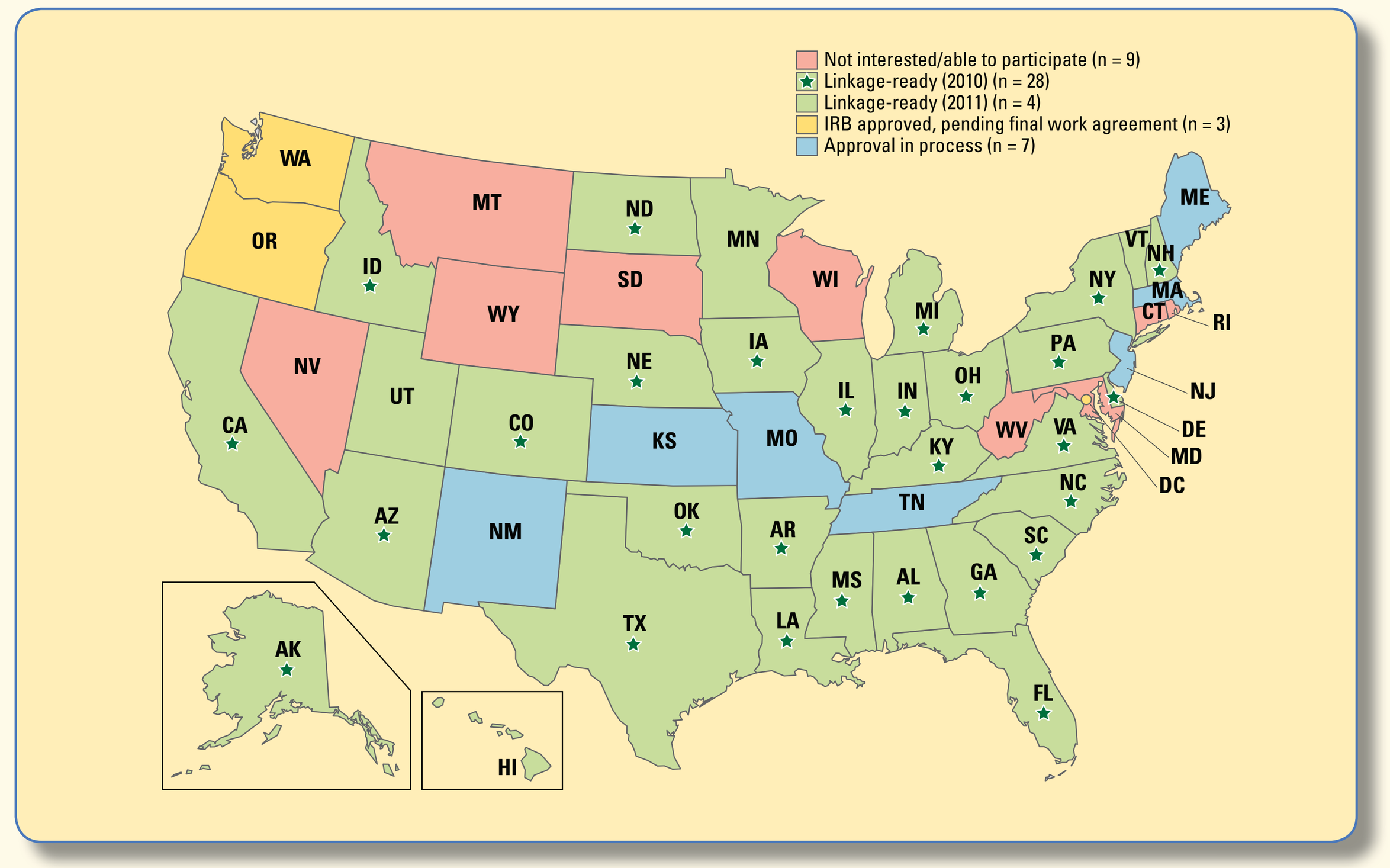
- All 50 states plus the District of Columbia were invited to participate. Figure 3 describes the results of the initial effort to identify and enroll states interested in participating.
- The understanding of study approval requirements locally by the registries and RTI evolved over time (from the initial expression of interest to "linkage-ready" status) and resulted in an iterative process to obtain necessary approvals.
- RTI was able to use the core standardized text for the required registry submissions; however, the level of detail and wording had to be extensively customized, adapted, and reorganized to accommodate the required format specific to each registry.
- 28 states completed all necessary requirements in time for the 2010 linkage. However, one registry was not able to participate in the linkage due to resource constraints.
- The average time from submission of the first application to the date the registry was linkage-ready was 94 days (range: 10 days to 195 days) (Figure 4).

Figure 4. Time From First Submission to Linkage-Ready Status for Cancer Registries That Participated in the 2010 Data Linkage



- Interested registries not able to complete the process before the first linkage continue to work with RTI to complete approvals needed to participate. Figure 5 displays a map of the state cancer registries and their status of participation as of May 15, 2011.

Figure 5. Map of Forteo Registry Participation as of May 15, 2011



Linkage

- In September 2010, the first annual linkage was completed between the Forteo Patient Registry database and cases of osteosarcoma diagnosed since January 1, 2009, from 27 participating state cancer registries (which covered 70% of the adult US population).
  - 6,338 patients from the Forteo Patient Registry were linked with a total of 431 adult osteosarcoma cases.
  - No matches were found.
- Due to the 9- to 18-month lag time between the date of cancer diagnosis and date the case is included in the state cancer registry databases, the osteosarcoma cases included in this first annual linkage are a subset of all osteosarcoma cases diagnosed in 2009 and 2010 in these registries, and additional 2009 and 2010 cases will be included in future linkages.

CONCLUSIONS

- The results of the first linkage with Forteo Patient Registry data indicate that it is feasible for a large number of states to perform a data linkage concurrently, using a standard data linkage algorithm.
- There are substantial challenges in obtaining approvals to conduct a study with many state cancer registries, because the same core information package detailing the study design, methods, and human subjects protections must be customized for many different review committees, using unique review criteria.
- Effective communication and collaboration between the researcher and cancer registry is essential for successfully navigating the variety of review and approval requirements that may evolve over time.
- A standardized research application and approval process for all state cancer registries would be extremely helpful to researchers and registries that wish to collaborate on similar studies, furthering our knowledge about the long-term safety of medications.

Lessons Learned

- Population-based studies that use data from state cancer registries play a significant role in drug safety surveillance activities. The opportunity for further collaboration is high, paralleling the public and regulatory interest in the long-term risk of cancer asssociated with many new therapies.
- In the absence of a national cancer registry with patient-level identifying data in the US, many studies will require participation of multiple statewide cancer registries.

REFERENCES

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2. Harris DH, Midkiff K, Gilsenan A, Andrews E. Public health surveillance collaboration: establishing a linkage algorithm with cancer registries for the Forteo patient registry. Poster presented at the North American Association of Central Cancer Registries Annual Conference; June 2010. Quebec City, Quebec, Canada.

DISCLOSURE

This study is sponsored by Eli Lilly and Company, however RTI-HS retains independent right to publish.

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