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Biosimilars for Healthcare Professionals

Naming and labelling of biologicals – the perspective of hospital and retail pharmacists

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Introduction: To date, the US Food and Drug Administration (FDA) has offered only draft guidance on the naming of biosimilar medicines. The Alliance for Safe Biologic Medicines (ASBM) has asked pharmacists for their views on the labelling and naming of biosimilar medicines.
Study objective: To determine the opinions of pharmacists about labelling and naming of biosimilars.
Methods: A total of 3,525 pharmacists in the US were invited to complete a survey on the naming and labelling of biologicals. Responses were received from 849 pharmacists, of which 401 completed the survey. Of the pharmacists who completed the survey, 60% worked in hospitals or the healthcare system, 40% worked in retail. Pharmacists were asked for their feedback on a recent FDA non-proprietary biologicals naming proposal. They were also asked what information they would like to see included in a biological product label in order to choose between multiple biosimilars and their reference products.
Results: Of the 401 pharmacists who completed the survey, 68% responded that FDA should require a distinct non-proprietary scientific name for every biological product – originator or biosimilar – approved by them. A total of 77% of respondents thought that a manufacturer-specific suffix should be included in the name of each biological product. Respondents considered the following as very important for label inclusion: clinical data to support whether or not the product was a biosimilar and whether or not the biosimilar and originator are interchangeable. Noting that the drug was a biosimilar was considered the most important; whether or not it was interchangeable was slightly less important.
Conclusion: A total of 401 pharmacists (11.4% of all those invited) completed the survey. The respondents comprised of 241 hospital pharmacists (60%) and 160 retail pharmacists (40%). Of these the majority of total respondents (68%) think that originator biological and biosimilars should have distinguishable non-proprietary scientific names and 77% think the name should include a unique, distinguishing suffix specific to the manufacturer for future product approval.

Keywords: ASBM, biologicals, biosimilars, labelling, naming, US FDA

Introduction

The market uptake of biosimilars in the US and worldwide will depend on regulatory policies [1], for which an agreed naming and labelling system will be important [2]. A survey of the views of European physicians on familiarity of biosimilar medicines demonstrated the need for distinguishable non-proprietary names to be given to all biologicals [3]. This has been supported by a number of discussions surrounding the development of clear regulation in this area [4-7], and a number of countries across the globe from Latin America [8, 9], Australia [10] and beyond; have called for specific nomenclature to be developed. The results of these surveys reinforce the value of a global naming policy for biologicals and the importance of the World Health Organization (WHO) moving forward with its biological qualifier proposal.

Since the US Food and Drug Administration (FDA) has only distributed draft guidance on the naming of biological medicines [11] and biosimilar labelling [12, 13], feedback from the pharmacists who prepare and dispense them is also important in determining how these drugs are regulated. In Europe, product labelling is seen as important to build user confidence in biosimilars [14]. In response to concerns in Europe, the Alliance for Safe Biologic Medicines (ASBM) invited 3,525 pharmacists in the US to complete a survey that included questions related to the information that could be included in a label, such as whether or not the product was a biosimilar; what analytical/clinical data and clinical similarity data should be present; post-marketing data; approved and non-approved indications; data source; and whether or not it was interchangeable/substitutable.

FDA has proposed a new policy that would require every biological – whether originator or biosimilar – to have a distinct non-proprietary scientific name. Both pharmacists and prescribers concluded that FDA was right to require a distinct non-proprietary scientific name for every biological product – originator or biosimilar – that FDA had approved.

Methods

In 2015, the ASBM invited 3,525 pharmacists in the US to complete a survey on the naming of biological medicines and biosimilar labelling [15], including feedback on FDA draft guidance on non-proprietary biologicals naming [11]. A total of 849 pharmacists replied (a response rate of 24%). Of these, 448 pharmacists were screened out predominately for their lack of knowledge on biologicals or did not complete the survey. A total of 401 pharmacists (11.4% of all those invited) completed the survey, and are collectively termed 'respondents'. Pharmacists were reimbursed US$22 for completing the survey.

Pharmacists were recruited from a large, global panel of healthcare professionals and were either employed in a hospital/health system pharmacy (60%) or retail pharmacy setting (40%). All 401 pharmacists that completed the study had dispensed biological medicines and had been in practice as a pharmacist for one year or more, see Figure 1.

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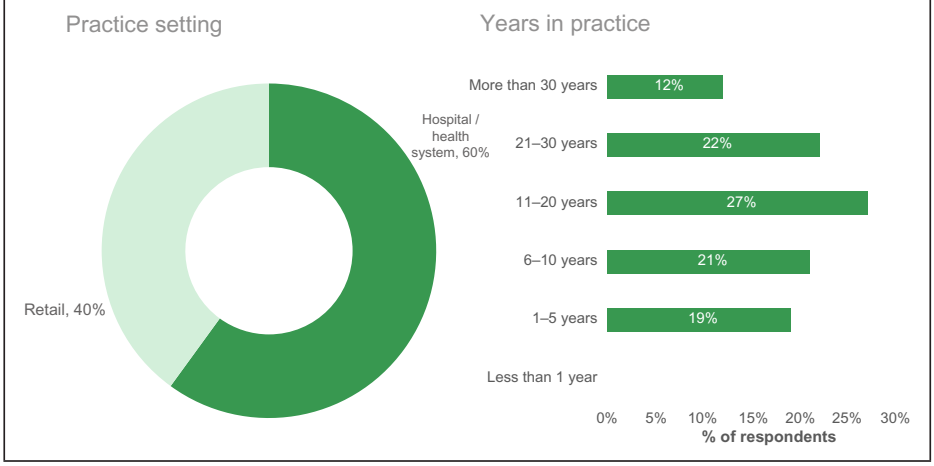
Figure 1: Professional experience of pharmacists included in the survey



Pharmacists were asked what information they would like to see included in a biological product label in order to choose between multiple biosimilars and their reference products. Data were analysed using MS Excel, and checked manually.

Results

Use of biological product reference material by pharmacists

The majority (64%) of pharmacist respondents were very familiar with the FDA 'Orange Book' [16], that is, the resource for Approved Drug Products, with Therapeutic Equivalence Evaluations. The 'Orange Book' is a reference that identifies drug products approved on the basis of safety and effectiveness by FDA. One third (29%) of pharmacists refer to this at least weekly, 24% monthly, 6% daily, with the rest referring to it less frequently. In contrast, 28% of respondents had never heard of the FDA 'Purple Book' [17], that is, the resource for Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations, and almost 80% of respondents never or infrequently used or referred to it. Information contained in the Purple Book is designed to help enable a user to see whether a particular biological product has been determined by FDA to be biosimilar to or interchangeable with a reference biological product. The results from the survey are outlined below and presented in Tables 1 and 2. Only 2% of pharmacists used the Purple Book daily, 7% of pharmacists used it weekly, 12% of pharmacists used it monthly, 30% of pharmacists used it rarely, and 49% of pharmacists never used the Purple Book at all.

Knowledge of biosimilars

Survey participants were asked how familiar they were with biosimilar medicines with the following question:

'Biosimilar medicines are intended to be copies of already approved biological medicines. They are referred to as "biosimilar" rather than "generic" because they will be similar, but not identical to the product they copy. How familiar are you with biosimilar medicines?'

Of the pharmacists who completed the survey, 57% of respondents said that they were familiar with biosimilars having a basic understanding and 35% said they had a complete understanding. Hospital pharmacists included in the survey reported being the most familiar with biosimilars, with 44% saying they had a complete understanding, while only 23% of retail pharmacists reported having a complete understanding.

Pharmacists were asked about their knowledge of the approval process for biosimilars using the following question:

'Originator medicines are approved by the US Food and Drug Administration based on an evaluation of clinical data that demonstrates a medicine is safe and effective for the specified indication and data must be provided for every indication. The approval pathway for biosimilars is different than for originator medicines. Are you aware a biosimilar medicine may be approved for several or all indications of the reference product on the basis of clinical trials in only one of those indications?'

Table 1: Respondent pharmacists' answers to survey on biologicals naming and labelling

Question	Answer	% Pharmacists
Should FDA require a distinct non-proprietary scientific name for every biological product – originator or biosimilar – approved by them?	Yes	68
	No	23
	No opinion	8
Should a random or a representative suffix be included in the name of every biological product?	Random suffix	15
	Manufacturer suffix	77
	No opinion	8
For purposes of accurately identifying the medicine, a representative suffix – for example, one that resembles the manufacturer name – is preferable	Completely agree	47
	Somewhat agree	38
	No opinion	6
	Somewhat disagree	7
	Completely disagree	1
For purposes of accurately identifying the medicine, I prefer a suffix that is a random 4-digit string of characters	Completely agree	7
	Somewhat agree	21
	No opinion	11
	Somewhat disagree	31
	Completely disagree	30

The responses suggest that overall knowledge among respondents was good with 86% answering yes (91% hospital pharmacists are more likely to respond 'Yes' versus 78% retail pharmacists). When asked if they thought that their understanding of the biosimilar approvals process was acceptable, there was a consensus that this was 'acceptable' (27%) or at least 'somewhat acceptable' (51%).

Naming knowledge

The survey participants were asked questions about their knowledge of the naming of biosimilars and what this meant about how these products could be used. Most respondents (63%) indicated that if biological medicines have the same non-proprietary scientific name, this would imply that the products are identical, with 68% hospital pharmacists are more likely to answer 'Yes' versus 57% retail pharmacists. Those respondents would expect the same results from biological medicines with the same non-proprietary scientific name. The majority of respondents (58%) believed that products sharing non-proprietary scientific names could be safely switched from a reference biological medicine to its biosimilar during a course of treatment and the same result would be expected with either of the products. When the same non-proprietary scientific name is used in two biological medicines, 55% of respondents would also assume that the medicines had both been approved for the same indications.

Naming requirements

When questioned about how biological naming should be regulated, the majority (68%) of the respondents thought that each product – originator or biosimilar – should have a distinct/unique non-proprietary scientific name. Furthermore, 77% of respondents thought the suffix on a biological medicine name should indicate its manufacturer, rather than a random suffix in future product approvals.

Biosimilar labelling

A total of 58% of respondents thought that it was very important that a product label for a biosimilar clearly indicates that it is a biosimilar. They also agreed that labels should include an explanation as to what a biosimilar is. Analytical information resulting from biosimilarity studies should be included, as should any clinical data submitted to FDA and any post-marketing data. There was also a consensus that the label should include reference to the brand name of the originator product.

Participants felt strongly that it should be clear and explicit on the label if a biosimilar product has not been approved for all indications approved for use of the reference product. The label should clearly distinguish data generated from the use of the biosimilar sponsor and that generated by

Table 2: Responses from respondent pharmacists to biosimilar naming and labelling survey (5: very important; 1: not at all important)

How important is it that	Score	% Pharmacists
a product label for a biosimilar clearly indicates that it is a biosimilar?	5	58
	4	23
	3	13
	2	2
	1	2
a product label for a biosimilar defines what biosimilarity means?	5	37
	4	30
	3	20
	2	10
	1	3
the biosimilar label includes the analytical data developed by the biosimilar sponsor to demonstrate its analytical similarity to the reference product?	5	34
	4	37
	3	19
	2	8
	1	2
the biosimilar label includes the clinical data, if any, submitted to FDA by the biosimilar sponsor to demonstrate that it is highly similar to the reference product	5	35
	4	36
	3	17
	2	8
	1	3
post-marketing data related to the biosimilar be added to the biosimilar label?	5	33
	4	32
	3	24
	2	8
	1	2
the label mentions the reference product by brand name so as to clarify the precise relationship between the originator product and the biosimilar product?[1]	5	36
	4	35
	3	19
	2	5
	1	4
the label explicitly states that specific indications or conditions of use that are approved for the originator product are NOT approved for the biosimilar product?[2]	5	48
	4	28
	3	16
	2	5
	1	3
the label clearly distinguishes those data generated by the biosimilar sponsor from those generated by the originator sponsor?	5	34
	4	35
	3	21
	2	6
	1	3

(*Continued*)

Table 2: Responses from respondent pharmacists to biosimilar naming and labelling survey (5: very important; 1: not at all important) (*Continued*)

How important is it that	Score	% Pharmacists
the label includes all relevant clinical similarity data, including clinical immunogenicity findings, from the biosimilar product development?	5	33
	4	35
	3	23
	2	7
	1	2
the label makes clear which indications were studied by the biosimilar sponsor and which indications were approved based on extrapolation from studies in other indications?	5	43
	4	33
	3	17
	2	4
	1	3
a product label clearly indicates a biosimilar is or is not interchangeable, meaning it may be eligible for automatic substitution by a pharmacist depending on the state in which the prescription is written?	5	64
	4	24
	3	8
	2	2
	1	2

[1]There were some differences among pharmacists depending on the practice setting in which they work. In response to the question 'How important is it that the label mentions the reference product by brand name so as to clarify the precise relationship between the originator product and the biosimilar product?', pharmacists in the community setting had a higher than average rating of importance for this (4.14) compared with pharmacists who work in the hospital setting (3.79).

[2]In response to the question 'How important is it that the label explicitly states that specific indications or conditions of use that are approved for the originator product are NOT approved for the biosimilar product?' pharmacists in the community setting had a higher than average rating of importance for this (4.32) compared with pharmacists work in the hospital setting (3.98).

the originator sponsor, and that it is clear which indications were studied with the biosimilar sponsor and which indications were approved based on extrapolation from studies of the reference product. Respondents also felt that labels should clearly include all relevant data used to establish similarity and clearly indicate if the biosimilar is interchangeable with a reference product.

Discussion

The results of this survey of pharmacists are consistent with the results from a survey of physicians in Europe [3]. In both surveys, respondents believed that products sharing a non-proprietary name could be considered identical, could be expected to produce the same results, could be used interchangeably and would be approved for all the indications of the reference product.

Many of the findings in this study support a recent survey sponsored by the Academy of Managed Care Pharmacy (AMCP) [18]. In the AMCP study, more than 60% of participants (62.3%) reported preferring a biosimilar naming convention that uses either a designated suffix (48.1% of all participants) or prefix (14.2% of all participants). Of the 48.1% who would prefer a designated suffix, the vast majority (83.4%) wanted a suffix that was based on the name of the manufacturer. In this survey, 77% of pharmacists expressed a preference for a suffix based on the manufacturer.

To date, FDA is yet to finalize its guidance for the naming of biologicals and labelling of biosimilars. This is a fast-evolving area – following publication of its draft guidance in 2015 and 2016 [11, 12], FDA issued a request for comments on expanding the number of suffixes that biosimilars makers could propose. The request was swiftly withdrawn; following what FDA said was an administrative error [19]. Some have speculated that the agency wanted to extend the comment period, which was originally in July 2016.

The results from surveys like the one described here will aid in the development of a clear and comprehensive system to promote the safe and effective use of biologicals and biosimilars, and as a result facilitate consumer confidence and market uptake in the US.

Conclusion

The pharmacists responding to this survey reported having a good overall knowledge of biosimilars and their approval process. The results suggest that when a biosimilar and the reference product share the same non-proprietary scientific name, it could lead to confusion among pharmacists. This is because two products sharing a non-proprietary name could be considered identical, be expected to produce the same results from both drugs, be used interchangeably, and be approved for all of indications of the reference product. As these are assumptions that cannot be made with biosimilars, pharmacist respondents agreed that all biological products should have unique names and that clear and explanatory labelling of these products should be required.

In general, all issues raised with regards to labelling were considered by pharmacist respondents to be very important for label inclusion. This means that they are supportive of biosimilar products being labelled specifically as such, with the clear inclusion of what a biosimilar product is. There should also be clear information about the analytical studies and clinical studies used for the approval of the product. In cases where the biosimilar is not approved for all indications of the reference product, this should be clearly indicated where

Key points of the 2015 pharmacists naming and labelling survey

- All items queried in the labelling survey were considered very important for label inclusion
  - The fact that a drug was a biosimilar was considered the most important; whether or not it was interchangeable was slightly less important.
- 68% of pharmacist respondents thought FDA should require a distinct non-proprietary scientific name for every biological product – whether originator or biosimilar – that FDA had approved. 23% of pharmacists did not, and 8% had no opinion.
- 77% of pharmacist respondents would prefer a suffix on the non-proprietary name, which is indicative of the product's manufacturer; only 8% of pharmacists had no opinion. 15% of pharmacists thought a random suffix that does not indicate the manufacturer – as recently proposed by FDA – would be best.

these indications are based on extrapolation of the indications approved for the reference product, and whether the biosimilar is interchangeable.

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