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ORIGINAL ARTICLE

# Survey of coagulation factor concentrates tender and procurement procedures in 38 European Countries

B. O'MAHONY,*†‡ D. NOONE*† and L. PRIHODOVA†§
*European Haemophilia Consortium, Brussels, Belgium; †Irish Haemophilia Society; ‡Trinity College, Dublin,Ireland; and §School of Psychology, University College, Dublin,Ireland*

**Introduction:** Procurement of coagulation factor concentrates (CFCs) for the treatment of haemophilia is a vital process that determines the quantity and quality of factor replacement therapy. **Aim:** The aim of this study was to examine the different tender and procurement systems used in Europe for the procurement of CFCs and the outcomes produced by the various systems. **Methods:** The survey questionnaire consisted of 30 items and explored various aspects of the procurement process including the prices of CFCs. In 2014, the survey was sent out by the European Haemophilia Consortium (EHC) to 45 national haemophilia patient organizations affiliated to the EHC in all European countries as well as to a designated clinician familiar with the procurement process. **Results:** The survey was completed by 38 European countries. Nineteen countries use a tender process, 17 an alternative procurement process and 2 use a combination of methods. A wide variety of agencies and individuals are involved in the process. Factors associated with optimum outcome and lower prices include a tender process with a specific legal framework and a tender board including haemophilia clinicians and patient organization representatives. Safety was reported as the most important selection criterion but given the safety profile of almost all currently licensed products, price was the main criterion used in many countries. **Conclusion:** The involvement of both clinicians and patient organizations greatly improves the outcome of a tender or procurement process, as does the presence of a legal framework that governs the process.

**Keywords:** factor concentrate, procurement, tender

## Introduction

Procurement of coagulation factor concentrates (CFCs) for the treatment of haemophilia is a vital process as the outcome determines the quantity and quality of factor replacement therapy available for the treatment of people with haemophilia. Availability of CFCs in Europe varies enormously, with reported use of factor VIII (FVIII) per capita varying from 0.1 IU per capita in Armenia to 8.56 IU per capita in Sweden and reported use of FIX per capita varying from 0 IU per capita in Armenia to 2.66 IU per capita in Ireland in 2012 [1]. The procurement legal framework for member states of the European Union is the Directive 2004/18/EU [2]. This applies to tenders carried out by government department or agencies funded substantially by government. Under this directive, tenders can be open, restricted, competitive dialogue or negotiated. For CFCs, an open call for tender would be the normal method unless there was only one possible supplier where a negotiated procedure may be used. The directive stipulates a clear framework for every step in the process. This directive will be replaced by a new EU directive 2014/24/EU [3], which has to be transposed into national law no later than April 17, 2016 (ironically World Haemophilia Day). The new directive will make tender systems more attractive by shortening the time period for submissions, mandating a move to full electronic submission of tenders and allowing for a degree of competitive dialogue as part of an open tender process. The aim of this study was to examine the different tender and procurement systems used in Europe for the procurement of CFCs.

Correspondence: Brain O'Mahony, Irish Haemophilia Society, First Floor, Cathedral Court, New Street, Dublin 8, Ireland.
Tel.: +353-1-6579900; fax: +353-1-6579901;
e-mail: brian@haemophilia.ie

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## Materials and methods

The questionnaire was designed by authors and circulated for review by the board of the European Haemophilia Consortium (EHC). The respondents were requested to provide answers to 30 questions explor-

ing various aspects of the procurement process including the prices of CFCs. The survey was sent out by the EHC to 45 national haemophilia patient organizations affiliated to the EHC in all European countries as well as to a designated clinician familiar with the procurement process in each country. Additional information was sought from the patient organizations, clinicians or publicly accessible documents, such as government websites if there was a need for any clarification. The data collection was carried out in 2014. The IBM SPSS 20 (IBM company, Chicago, Illinois, USA) was used to carry out the descriptive and explorative analyses (ANOVA, *t*-test).

## Results

Responses were received from 38 countries, with response rate of 84.4%. The surveys were completed by the clinicians in seven countries (18.4%), by the National Haemophilia patient organisations by 20 (52.6%) and by both in 11 (29%). Nineteen countries reported using a tender (50%), 17 reported an alternative procurement process (44.7%) and 2 reported using a combination of a tender and alternative procurements process (5.3%) (Table 1).

## Tender process

### *Tender committees and framework*

All 19 countries that use a tender process, have a legal framework or law that governs the tender process. Ten are EU member states and therefore come under the jurisdiction of the EU procurement directive [2]. Fifteen have a national tender, two have hospital-based tenders and one has a combination of national

**Table 1.** Overview of tender and alternative procurement processes.

| | Tender procurement process | Alternative or combined procurement process |
|---|---|---|
| *N* | 19 | 19 |
| Countries | Albania, Azerbaijan, Belarus, Bosnia & Herzegovina, Czech Rep, Denmark, Hungary, Ireland, Moldova, Montenegro, Poland, Portugal, Romania, Russia, Serbia, Slovak Rep., Slovenia, Ukraine, United Kingdom | Austria, Belgium, Croatia, Estonia, Finland, France, Germany, Greece, Italy, Kyrgyzstan, Latvia, Netherlands, Norway, Spain, Sweden, Switzerland, Turkey. Combined – Bulgaria, Lithuania |
| *Committees and framework* | | |
| Tender/procurement boards | 16 | 8 |
| Legal framework | 19 | 15 |
| Written terms of reference | 10 | 4 |
| Mean term of office | 2.3 years | 1.5 years |
| Mean contract duration | 1.4 years | 1.9 years |
| Clinician involvement | 15 | 11 |
| Patient organization Involvement | 8 | 6 |
| *Tender/purchase details* | | |
| pdFVIII | 18 | 17 |
| pdFVIII + VWF | 13 | 18 |
| rFVIII | 16 | 18 |
| pdFIX | 17 | 18 |
| rFIX | 8 | 14 |
| PCC's | 11 | 14 |
| CFCs | 11 | 16 |
| RBD products | 7 | 13 |
| Publish call for tender | 16 | NA |
| Publish criteria with the call for tender | 15 | NA |
| Patients can stay on current product | 6 | NA |
| *Criteria* | | |
| Safety | 14 | 9 |
| Efficacy | 12 | 10 |
| Quality | 12 | 8 |
| Convenience | 8 | 3 |
| Security of supply | 10 | 6 |
| Price | 18 | 12 |
| *Ranking* | | |
| | Safety | Safety |
| | Price | Efficacy |
| | Efficacy | Price |
| | Other* | Other* |
| | Quality | Supply |
| | Supply | Convenience |
| | Convenience | Quality |

pdFVIII, plasma-derived factor VIII; rFVIII, recombinant FVIII; VWF, von Willebrand factor; Prothrombin Complex Concentrates, PCC's; CFC, coagulation factor concentrate, Rare Bleeding Disorder (RBD).

*Eight countries for tender countries listed also other criteria, such as country of origin, technical and scientific support, dosage, inhibitor risk and continuity of product for an individual. For alternative countries, Estonia use other criteria based on plasma sale contracts.

 

and hospital-based tenders. Bosnia and Herzegovina, have a variation on a national tender.

Table 2 shows the key representative bodies, which have formal involvement on the tender committee or boards. With the exception of Azerbaijan, Hungary, Poland, all have a tender committee or board for haemophilia products. The level of clinician/haemophilia centre involvement as well as patient involvement in the tender process varies across the 19 countries. Other members of tender committees formally involved in different countries include a virologist, a procurement agency, a blood safety expert, a regulator and a clinician from the national registry. The mean term of office for members of the tender board is 2.3 years with the minimum being 2 months in the Slovak Republic and the maximum being 6 years in Russia. Ten countries have written terms of reference for the tender committee. When contracts are awarded, in tender countries, seven reported that one company was awarded the tender and 12 countries reported that the contracts were awarded to multiple companies. No effect was observed on price where the contract was awarded to one or more than one company.

### *Alternative procurement process*

Seventeen countries reported using an alternative procurement process that is not a tender, all of which were highly varied. In Latvia, products are purchased nationally if they are included in a reimbursement list. There are several lists and the majority of factor concentrates are included in list A where the government pays for the least expensive therapy and a patient who wishes to use a different product has to pay the difference in cost. The decisions are made by individual hospital boards in the Netherlands, and by state agencies involved in the procurement in Spain, Turkey, Switzerland and Kyrgyzstan. In Sweden, purchasing is overseen by the Dental and Pharmaceutical Benefits Agency (TLV) and in France by hospitals. In France and Belgium, all licensed products must be available and this mitigates against using a tender system. In Finland, companies apply to the national health authorities for inclusion of their products for reimbursement. In Croatia, factor concentrates are made available under the expensive drugs budget. In Germany, haemophilia treatment centre hospitals and clinicians decide which products should be used and these are then reimbursed by health insurance. In Estonia, purchase of factor concentrates in two hospitals is linked by the hospitals to the sale of donor plasma.

Bulgaria and Lithuania use a combination of both tender and alternative procurement processes. For the purpose of analysis, the countries reporting alternative procurement and combination procurement processes were combined.

### *Committees and framework*

Of the 19 countries with an alternative procurement process, 15 countries have a legal framework or law that governs the procurement process, 3 countries reported no legal framework governing the procurement of products for haemophilia (Netherlands, Greece and Germany). Norway did not respond.

A number of different organizations or authorities are responsible for the procurement of products for haemophilia (Table 3). Hospitals are responsible in six countries, ministries of health or regional government in seven countries, specific medicines agencies or pharmacies in three countries, health insurance funds

**Table 2.** Organizations involved in tender boards.

| | Health insurance funds | Medicines agencies or pharmacies | Hospitals or blood centres | Ministries of Health | Clinicians or Haemophilia Centres | Patient organization |
|---|---|---|---|---|---|---|
| Involved in all aspects of the process | Bosnia. & Herzegovina. Hungary Montenegro, Serbia Slovak Rep. | Denmark United Kingdom Azerbaijan Romania Belarus | Albania Czech Republic Ireland Portugal Romania | Albania Azerbaijan Belarus Ireland Russia | Ireland Denmark Montenegro Serbia United Kingdom | Ireland Serbia |
| Involved only in scientific and technical aspects of the process | | | | | Romania Portugal Bosnia. & Herzegovina. Moldova | Portugal Slovenia United Kingdom |
| Informally involved or observer status | | | | | Azerbaijan, Hungary, Czech Republic, Romania and Ukraine | Hungary, Slovak Rep., Bosnia. & Herzegovina, Ukraine, Moldova |
| Not involved | | | | | Poland, Russia | Azerbaijan, Czech Rep., Romania, Poland, Russia, Belarus, Albania, Denmark, Montenegro |

**Table 3.** Organizations involved in alternative procurement process.

| | Health insurance funds | Medicines agencies or pharmacies | Ministries of Health or local authorities | Clinicians or Haemophilia Centres | Patient organization |
|---|---|---|---|---|---|
| Involved in all aspects of the process | Kyrgyzstan Croatia | France Belgium Kyrgyzstan Sweden | Kyrgyzstan Italy | | Kyrgyzstan |
| Involved only in scientific and technical aspects of the process | | | Turkey | France Kyrgyzstan Estonia | |
| Informally involved or observer status | | | | Austria, Bulgaria, Estonia, Germany, Greece, Lithuania, Italy, Norway and Spain | Croatia, France, Lithuania, Spain |
| No involvement | | | | Finland, Belgium, Croatia, Turkey, Switzerland, Netherlands, Latvia | Turkey, Sweden, Estonia, Finland and Belgium, Austria, Germany, Greece, Latvia, Netherlands, Norway, Switzerland, Bulgaria |

in two countries. Eight of the 19 countries have a procurement committee or board involved in the process and 10 have reported that they do not. Unlike the countries using a tender system, only 42% of countries using an alternative process have a committee or board for the selection of haemophilia products. Other additional members involved in the board include procurement agencies, social security institutions or the ministry of finance.

### *Procurement method and CFC prices*

Table 4 reports the breakdown of the countries that reported pricing and assessed for variance between tender procurement and alternative process. There was a reduction in price in the procurement cost of recombinant FVIII (rFVIII; $P = 0.05$), plasma-derived FVIII (pdFVIII) and pdFIX ($P = 0.01$) when a tender process is used.

In relation to patient organization and clinician involvement and cost of factor concentrates a difference was also noted. For every category of product, patient organization involvement resulted in lower prices paid for factor concentrates (Fig. 1) with a statistically significant difference in the price of rFVIII between a mean price $IU^{-1}$ of € 0.55 (±€ 0.16) when involved to a mean of € 0.72 (±€ 0.22) when they are not involved ($P = 0.05$). A similar, though less marked, effect is observed for the involvement of clinicians (Fig. 2). Mean prices are lower when clinicians are involved for rFVIII and rFIX, with no difference for pdFIX and for pdFVIII.

When asked if there was a specific legal framework or law that governs the tender or procurement process (Fig. 3), there was a trend of reduced price $IU^{-1}$ across all CFCs if there was a legal framework. This difference was statistically significant for pdFVIII ($P = 0.05$) and pdFIX ($P = 0.01$).

The mean duration of a contract is greater with alternative procurement processes at 1.9 years compared to tender processes at 1.4 years. In countries using a tender system, 83% use a registry to predict the supply required with the majority using national registries and 2 using hospital registries. This is in contrast to the countries using an alternative procurement process with only 5 (27%) using a registry to predict supply of product.

## Discussion

In this survey, 19 countries reported the use of a tender system with 17 using an alternative procurement system and 2 using a combination of systems. The previously outlined arguments in favour of national

**Table 4.** Median prices in countries using tender or alternate procurement processes.

| | Tender | | | Alternative procurement | | |
|---|---|---|---|---|---|---|
| | Countries (*N*) | Median (€) | Range (€) | Countries (*N*) | Median (€) | Range (€) |
| rFVIII | 12 | 0.56 | 0.28–1.05 | 17 | 0.69 | 0.39–1.06 |
| pdFVIII | 15 | 0.40 | 0.16–1.16 | 16 | 0.64 | 0.18–0.90 |
| rFIX | 6 | 0.73 | | 12 | 0.72 | |
| pdFIX | 15 | 0.40 | 0.18–0.83 | 17 | 0.54 | 0.38–0.88 |

pdFVIII, plasma-derived factor VIII; rFVIII, recombinant FVIII.

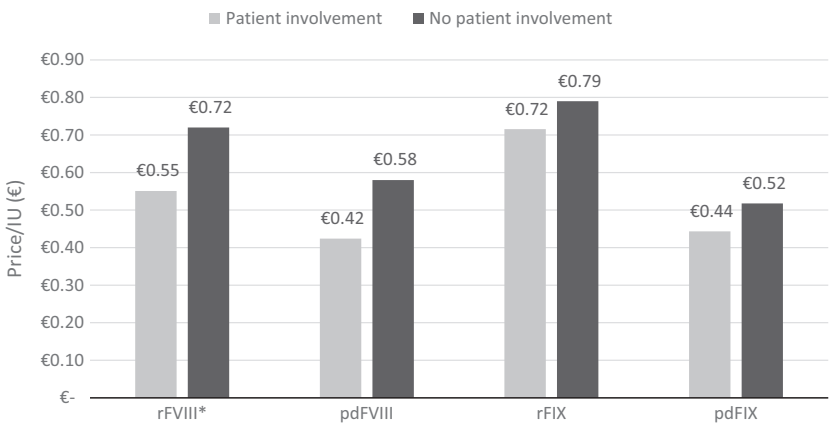


**Fig. 1.** Mean price $IU^{-1}$ of coagulation factor concentrates vs. patient organization involvement in procurement process. *$P \leq 0.05$.

* $P \leq 0.05$

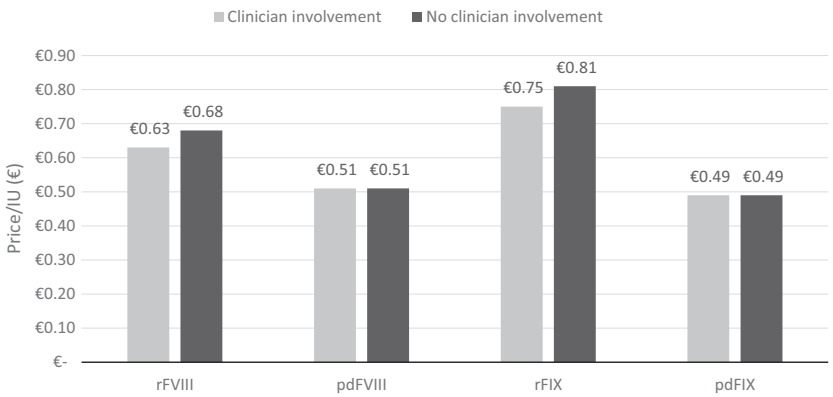


**Fig. 2.** Mean price $IU^{-1}$ of coagulation factor concentrates vs. clinicians involvement in procurement process.

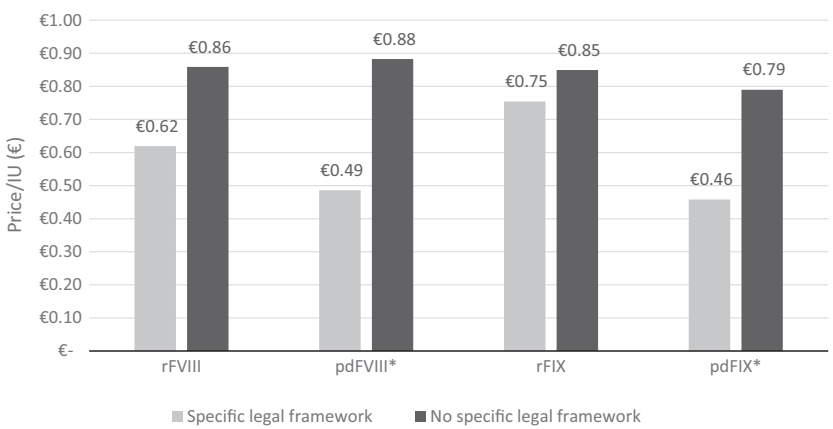


**Fig. 3.** Mean price $IU^{-1}$ of coagulation factor concentrates if a specific legal framework is used. *$P \leq 0.05$.

* $P \leq 0.05$

tenders include better evaluation and selection criteria that are agreed by all the key stakeholders, having all the appropriate experts make a collective decision, better prediction of national supply and demand and lower prices based on higher volume purchased amounts [4]. It has also been argued that competitive tender systems lead to lower prices for factor concentrates [4,5]. This point is clearly borne out by the results of this survey. In countries using a tender system when compared to an alternative system, the mean price of rFVIII products was 23% lower, the mean price of pdFVIII was 21% lower and the mean price of pdFIX was 30% lower. These are very significant reductions and in the case of rFVIII and pdFIX

these differences were statistically significant. There was no appreciable difference in the mean price of rFIX but this is hardly surprising given the fact that there was only one rFIX product licensed in Europe at the time of the survey. An open tender process would not be expected to result in cost reductions where there is only one suitable product and in this case a negotiated procedure can and should be used. All countries, which utilize tenders, reported doing so under a legal framework compared to 14 of the 19 countries, which use an alternative or combined. The survey demonstrates that in the absence of a legal framework, prices paid for CFCs tend to be higher.

In countries using tenders, 16 of the 19 use a tender or procurement board compared to 8 of the 19 using an alternative or combined method. The importance of the key clinicians and patient organizations involvement in any procurement process has previously been strongly emphasized [4]. In order to objectively assess the impact of this involvement, price was compared against the involvement of clinicians and patients both for the tender and alternative procurement processes. In tender countries, clinicians are involved in 15 of the 19 (79%) countries compared to 11 of the 19 (58%) using alternative procurement processes. The presence of clinicians on tender boards or with alternative procurement processes results in lower mean prices for most categories of products. The involvement of patient organizations has, however, even greater impact. In 8 of the 19 (42%) countries, which use a tender process, patient organizations are involved compared to 6 of 19 (31%) countries using an alternative procurement method. Patient organization involvement results in lower prices for all categories of products to a greater extent than seen solely with clinician involvement. This difference due to patient organization involvement is statistically significant in the case of rFVIII with a mean reduction in price of 24%. This is not surprising. Clinicians on a national tender board tend to be among the leading haemophilia clinicians in their country and experts in haemophilia. Patient organization representatives tend to be knowledgeable and committed to the best standards of haemophilia treatment. Where patient organizations are involved, clinicians are also involved. It is clear that the involvement of both clinicians and patient organizations greatly improves the outcome of a tender or procurement process. The knowledge and judgement that clinicians and patient organizations can bring to the process usually means better selection criteria being promulgated and a better more knowledge-based analysis of these criteria. Including the clinicians and the patient organizations demonstrates a commitment by governments and health authorities to an open, transparent and optimal process. In our survey for example, countries that involved patient organizations in the procurement process were more likely to have a legal framework governing the process than countries without involvement of patient organization (100% vs. 86.4%), along with written terms of reference (50% vs. 31.8%) and publishing of the call for tender (90.9% vs. 72.7%). Agreement between clinicians and patient representatives may ensure an establishment and enforcement of decisions, made on a more objective and agreed basis which result in increased competition, transparency and thereby optimize costs.

The formal involvement of clinicians in a tender process and the informal involvement of the patient organization in the United Kingdom have previously been reported and led to an almost 50% reduction in unit cost over a 6-year period [5]. Only two countries, Ireland and Serbia, have full formal participation by the patient organization in their national tender process. In Ireland, this involvement over the time period 2004–2014 has contributed to a reduction in the unit cost of rFVIII over that time period of 60% and a total reduction in cost of 70% when handling fees and associated charges were removed [6]. This has led to a stabilization of the haemophilia budget during a time when the FVIII per capita consumption increased from 3.2 to 8.2 IU per capita, and the country was experiencing a major economic downturn and very significant decrease (22%) in the national health budget [7]. This reduction in cost contrasts with 10 other European countries in this survey for which we have comparable price data for 2004 where there was no decrease in the mean price between 2004 and 2014.

Patient organization involvement demands a serious commitment and well-trained and knowledgeable patient organization representatives. The authors have been involved in training patient participants and indeed clinicians and health ministry officials from several countries for participation in tender processes [8]. In our view, any tender or procurement process, which excludes or does not specifically include key haemophilia clinicians and patient organization representatives, is deficient. In these cases, the decision can be taken by individuals with little or no knowledge of haemophilia whose sole motivation is to lower the price to the detriment of any real evaluation of safety, efficacy, quality or other relevant criteria. This situation has been the subject of representations by the EHC to the governments of two EU member states where the tender board has not included the clinical and lay expertize to properly evaluate the products [9,10].

Countries using tender procurement ranked safety as the most important criterion but 14 of the 19 listed price as the main criteria. The selection criteria used often include safety, efficacy, quality, security of supply and price. It may be the case that tender boards find small differences between several products in the same class (e.g. rFVIII or pdFVIII) and even though

 

safety may be the most important criteria, the deciding criteria may be price as the one criterion where there can be significant differences between products. In the United Kingdom rFVIII tender for 2010–2014, unit price constituted 75% of the total scored criteria [5]. In the Irish rFVIII tender for 2012–2014 price constituted 30% of the total but in both cases price was the most significant criteria in the final decision as the differences between the products on the other criteria were minimal. Setting safety and efficacy as the most important criteria allows a tender or a procurement board to decide not to purchase products which do not meet their standards for safety or efficacy and then prioritize other criteria such as price.

The reported prices of CFCs in this survey were either provided by the national patient organization or in some cases by a clinician or from publicly available documentation. In some countries the list price does not accurately reflect the prices paid as individual health authorities, insurance funds or hospitals may negotiate discounts on the quoted list price. This highlights the need for a greater transparency regarding the actual prices paid for CFCs in Europe.

Several studies have demonstrated no link between product switching and inhibitor risk following a tender resulting in a switch of products for the majority of patients [11–14]. The duration of tenders should not, however, be so short as to require very frequent switching. Alternatively, some tender systems allow for several products to be purchased thereby facilitating no requirement to switch products if required in defined cases such as patients with a previous history of inhibitors.

Tender and procurement selection criteria for CFCs will require rethinking when longer acting factor concentrates are licensed and available in Europe. One IU of longer acting factor will not be equivalent to one IU of currently available factor and additional factors will need to be considered in the procurement process, such as the difference in half-life or treatment protocols for the different products using prophylaxis or on-demand regimes. In the USA, the published average wholesale price for the first licensed longer acting rFVIII and rFIX [15] demonstrated that the unit price was increased almost in line with the reported extension in half-life. However, hospitals or payers very often secure discounts on these prices in the USA so the actual prices paid are not as clear. Furthermore, in Germany, high costs were generally incurred at market launch of a new medicinal product. To control this, the Act on the Reform of the Market for Medicinal Products, which entered into force in January 2011 is designed to regulate pricing of new medications and thus their eligibility for reimbursement in the German pharmaceutical market. Manufacturers need to demonstrate proof of an added benefit over a comparator therapy for all new medicinal products in order to benefit from any increase in price. If no added benefit is assigned by the Federal Joint Committee, then the price of a new product may not exceed the current reference price. Similar mechanisms are currently being evaluated by other European countries and the results of the new German system will be closely monitored.

New or novel methods of price and value comparisons may be required. Outcome-based pricing based on defined annual bleed rates, total cost of all the CFC requirements for a country, average annual cost per patient with severe Haemophilia are all possible mechanisms. The new EU directive, 2014/24/EU will assist in this process in Europe as there is provision for increased discussion under the competitive procedure with negotiation.

To our knowledge, this study is the first systematic attempt to analyse and compare various CFCs procurement methods carried out in Europe, with a high response rate (over 80%). On the other hand, when interpreting the statistically significant differences it is important to consider that the results were based on responses from 38 countries and therefore the effect of size on power cannot be entirely disregarded.

Future studies should be carried out in order to obtain more data on prices and nuances of country's procurement process. In addition, a detailed analysis of the evaluation criteria, specifically with the breakdown of the quality/safety/secure supply criteria, could provide a valuable insight in the variations in the procurement process outcomes and provide guidance for improvement of the criteria.

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All authors met at least one of the following criteria recommended by the ICMJE and have agreed on the final version.

## Disclosures

The authors stated that they had no interests which might be perceived as posing a conflict or bias.

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