Włodarczak U, Swieczkowski D, Religioni U, Jaguszewski M, Krysinski J, Merks P. Awareness of the implementation of the Falsified Medicines Directive among pharmaceutical companies' professionals in the European Economic Area. Pharmacy Practice 2017 Oct-Dec;15(4):1031.

https://doi.org/10.18549/PharmPract.2017.04.1031

**Original Research**

# Awareness of the implementation of the Falsified Medicines Directive among pharmaceutical companies' professionals in the European Economic Area

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Received (first version): 21-May-2017 Accepted: 16-Oct-2017 Published online: 20-Dec-2017

## Abstract

**Background**: The Falsified Medicines Directive (FMD) is a response of the European Union to the increasing number of falsified medicines present in the legal supply chain within the Member States of the community. Effective implementation of the new regulations will depend on the effective cooperation of all parties involved in the distribution of medicinal products including the managers of pharmaceutical companies.

**Objective**: The objective of the study was to examine awareness of the Implementation of the FMD among pharmaceutical company professionals in the European Economic Area.

**Methods**: Sampling was conducted using a method called purposive sampling. An appropriate research tool in the form of an original questionnaire was made available to the respondents in electronic form. During the period from January 2016 to June 2016, 1,496 e-mail messages were sent. The response rate was 17.37%.

**Results**: The study included 99 women (39.3%) and 153 men (60.7%). In the study group, 95.7% of people had heard of FMD. Doctors had rarely heard about the falsified medicine directive when compared to pharmacists (p=0.0063), people working in the pharmaceutical industry (p=0.0014), and respondents with a different professional profile (p=0.0114). In the study group, 89.6% of people were aware of the role of National Medicines Verification Organization in the process of implementing the provisions of FMD into the national system of distribution of medicinal products. The number of the respondents who knew the deadline for the implementation of FMD was significantly higher in the study population, i.e. 91.9% (p=0.0001). Both the younger respondents and those with lower level of education were less aware of the time requirements posed to national regulators (p=0.0003, p=0.0023, respectively).

**Conclusions**: Awareness of the regulations related to the implementation of the FMD, although relatively high among pharmaceutical company professionals in the EEA, is still insufficient.

## Keywords

Counterfeit Drugs; Health Services Accessibility; Professional Practice; Health Knowledge, Attitudes, Practice; Pharmacists; Surveys and Questionnaires; Europe



## INTRODUCTION

Falsified medicinal products represent one of the most significant challenges for global patient safety, and remain a key issue of public health at the beginning of the twenty-first century.[1-3] The struggle with the increasing number of falsified medicinal products affects the activities of all parties involved in drug distribution – manufacturers, wholesalers, community and hospital pharmacies; and on the other hand, presents challenges for policy makers responsible for the drug safety of the European Union (EU).[4,5] The fight against illegal places of pharmaceutical distribution is not only European domain, but it is also part of the global action initiated by the Food and Drug Administration (FDA).[6] While the phenomenon of the illegal trade of drugs outside the pharmaceutical distribution chain described in the law is a well-recognized matter, the scale of this phenomenon in the legal distribution remains poorly defined.[7,8] Current activities in the EU are focused directly on improving the safety of the pharmacotherapy of patients at the international level. This is done by monitoring drug distribution in countries belonging to the EU and introducing common mechanisms to verify the authenticity of pharmaceuticals in Member States.[9] This action is supported by the Council and the European Parliament's Falsified Medicines Directive and by implementing rules adjusted to this regulation – the so called Delegated Act, constitutes a joint effort of the EU to

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https://doi.org/10.18549/PharmPract.2017.04.1031

challenge illegal pharmaceuticals.[10-12] It is worth noting that according to EU rules, a falsified medication is any medicinal product which has been falsely presented in: i) identity of the product, including its packaging, labeling, name, or its' ingredients list, including excipients, and the strength of those ingredients, or ii) in regards to the country of origin, including the manufacturer, country of manufacture, and the holder of the marketing authorization, as well as the history of medicine's trading, including the records and documents related to the used channels of distribution. This definition does not include unintentional quality defects and is without prejudice to infringements of intellectual property rights.[13]

In the context of pharmacy practice, these new obligations will be introduced into routine settings, and can often be time-consuming for the staff of community and hospital pharmacies. However, it should be noted that due to the solutions proposed by the EU Parliament, the role of the pharmacist will increase. In particular, at the time of drug dispensing, the pharmacist will be required to scan the package's unique serial identifier in the form of a technologically advanced matrix, allowing them to check the authenticity of the drugs. This safety feature will be obligatory for all prescription drugs, as long as separate documents do not state otherwise. Moreover, some over-the-counter (OTC) drugs will have similar security regulations if they are listed in the delegated act. Apart from a unique identifier, the directive recommends implementing a mandatory security measure located on the external package (tamper evident feature) to protect the drug against undesired opening. The verification process – authentication - will therefore be nothing other than a basic element of pharmaceutical care, optimizing pharmacotherapy and increasing the level of patient safety.[14-16]

The actions described above are a great challenge for individuals responsible for drug policy who will be in charge of organizing the institutions that supervise these new regulations. It should be noted that at the European level this will be EMVO (European Medicines Verification Organization), and at the national level - NMVO (National Medicines Verification Organization). Their main task will be to create data repositories necessary to authenticate individual drug packaging.[17] The new amendments will be constituted in 2019 and new security measures should be introduced no later than the 9th of February 2019.[18,19]

Effective introduction of the described solutions depends to a large extent, on the awareness and knowledge of the managers of pharmaceutical companies, as no legal regulation can be effectively implemented without properly organized human resources. Pharmaceutical companies should take an active part in the implementation of the drug authentication system in the EU. The aim of our project was to investigate the awareness of pharmaceutical companies managers of the legal regulations related to the implementation of FMD. This work constitutes a unique voice in the discussion on the falsified medications trade within the legal distribution chain and the place of community pharmacies in the implementation of EU regulations.

## METHODS

### Sampling

Sampling was conducted using a method called purposive sampling. Its main purpose is to focus on the specific characteristics of the population which are the subject of interest, and which will answer the research questions best. Thus, the selection of the test group is based upon the individual judgment of the investigator. Having in mind the regulations provided by the FMD and the Delegated Act, we selected organizations and institutions involved in introducing new law into routine settings, among others, those dedicated to organizing NMVO, for instance, representatives of innovative or generics manufacturers, as well as individuals from marketing authorization holders. Finally, we included people who are integrated in the industry, wholesalers and pharmaceutical associations, bearing in mind the European context of the study. It should be noted that we based this list upon: i) data that is publicly available – we collected contact details from the official websites of the above-mentioned parties; and ii) data collected during meetings and conferences, both business and science-related – in this case, one of the members of the research team (PM) requested contact details from participants. It should be emphasized that all potential respondents were informed about the aim of the research study and were assured that all contact information would only be used in line with the aim of the study project and not forwarded to any different bodies who were unassociated with scientific questioning. Moreover, in the invitation sent to the respondents (via e-mail), we stated that completion of the questionnaire is associated with an official declaration of consent for participation in the study. To avoid collecting multiple data referring to one individual, we prepared a separate database. Whenever we found more than one e-mail for a certain person, we decided to use only one of the email addresses available. This decision was based mainly on the primary workplace of the respondent, e.g. in the case of individuals who work at both a university and in the industry, invitations were sent to the e-mail associated with a pharmaceutical company. We tried to avoid the use of private e-mail addresses and thus, only used them when participants provided this information along with their direct consent of its use during a conference. Before final approval of the database, a member of research team (DŚ) who was not involved in the collection of any contact information, checked the correctness and accuracy of the data acquired in the context of any spelling and/or punctuation mistakes (e.g. the lack of ‘dot’ and ‘at’) as well as repetition or other errors which could possibly lead to a decreased rate of response. All participants were advised of their right to withdraw their consent during the study period. The study was conducted respecting both the Polish and European law preserving the anonymity of respondents. This meant that any personal data was only available to the research team, and consequently, no identifying data was revealed during the analysis and release of the results of the study

https://doi.org/10.18549/PharmPract.2017.04.1031

Table 1. Socio-demographic characteristics of the respondents.

| | Men (n=153) | Women (n=99) | Sum (n=252) | p-value |
|---|---|---|---|---|
| Age | | | | |
| 21-29 | 4 (2.6%) | 4 (4.0%) | 8 (3.2%) | 0.0748 |
| 30-39 | 15 (9.8%) | 19 (19.2%) | 34 (13.5%) | |
| 40-49 | 52 (34.0%) | 33 (33.3%) | 85 (33.7%) | |
| 50-59 | 59 (38.6%) | 30 (30.3%) | 89 (35.3%) | |
| 60 and more | 23 (15.0%) | 13 (13.1%) | 36 (14.3%) | |
| Education | | | | |
| Primary education | 2 (1.3%) | 2 (2.0%) | 4 (1.6%) | 0,5961 |
| The level of single structure education | 1 (0.7%) | 1 (1.0%) | 2 (0.8%) | |
| General secondary education | 5 (3.3%) | 2 (2.0%) | 7 (2.8%) | |
| Secondary vocational education | 4 (2.6%) | 4 (4.0%) | 8 (3.2%) | |
| Post-secondary non-tertiary education | 15 (9.8%) | 4 (4.0%) | 19 (7.5%) | |
| Tertiary education | 126 (82.4%) | 86 (86.9%) | 212 (84.1%) | |
| Profession | | | | |
| Physician | 9 (5.9%) | 0 (0.0%) | 9 (3.6%) | 0.0140 |
| Pharmacist | 64 (41.8%) | 54 (54.5%) | 118 (46.8%) | 0.0482 |
| Employed in the industry | 50 (32.7%) | 20 (20.2%) | 70 (27.8%) | 0.0308 |
| Other specialties | 39 (25.5%) | 29 (29.3%) | 68 (27.0%) | 0.5066 |

**Research tool**

An appropriate research tool in the form of an original questionnaire was made available to the respondents in an electronic form using the public Internet service (survey tool). The questionnaire was divided into two sections. The first consisted of six questions, which allowed for the collection of information about the demographic and professional affiliation of the members of the study population. The second part had general questions related to the implementation of the FMD in the national and European context, as well as issues related to the EMVO and its national counterpart, NMVO. In the questionnaire both open and closed questions were used. They were based on the Likert scale with conjunctive and disjunctive choices. The questionnaire was distributed in English. The verification of linguistic correctness and style of the questionnaire was done by a team of experts from Poland and Great Britain. Information about the study and the research group was attached to each questionnaire. The study was preceded by a pilot study, designed to test the acceptability of the research tool on a 50-person group of respondents with a medical or pharmaceutical education (face validity). During this phase, respondents could provide comments about the questionnaire, particularly in the context of understandability. Finally, all comments were analyzed by the research group and used to improve the quality of the surveyed tool. During the period from January 2016 to June 2016, 1496 e-mail messages were sent. Forty five of these messages were not delivered due to technical reasons. Throughout the study, a reminder was sent up to four times to the individuals who did not reply. 252 responses were received. The response rate was 17.37%.

**Bioethics Commission**

The study received consent from the Bioethics Committee of the University of Nicolaus Copernicus in Torun (Poland) No 3/2016 KB at the Ludwig Rydygier Collegium Medicum in Bydgoszcz, a leading Polish medical university.

**Statistical Analysis**

All statistical calculations were performed using the statistical package StatSoft. Inc. (2014). STATISTICA version 12.0 and Excel spreadsheet. The quality variables are presented by frequencies and percentages. The significance of differences between the two groups (unrelated variables model) was examined by a test of the significance of differences: U Mann-Whitney test (for variables measured on an ordinal scale). The significance of differences among more than two groups was verified by Kruskal-Wallis test. In case of statistically significant differences between the groups, post hoc tests (Dunn's test) were applied. Chi-square tests of independence were used for categorical variables (by using Yates correction for the cell number below 10, checking the Cochran's conditions, Fisher's exact test). In all calculations for significance the level was set at p=0.05.

## RESULTS

The study included 99 women (39.3%) and 153 men (60.7%). The percentage of respondents aged 21-29 years was 3.2%, aged 30-39 years was 13.5%, aged 40-49 years was 33.7%, aged 50-59 years was 35.3% and above 60 years of age was 14.3%. In the study group, the level of education among the respondents was as follows: completed primary education 1.6%, the level of single structure 0.8%, general secondary education 2.8%, secondary vocational education 3.2%, post-secondary non-tertiary education 7.5% and completed tertiary education 84.1%. The study involved physicians (3.6%), pharmacists (46.8%), people employed in the industry (27.8%) and people from other specialties (27.0%). Respondents could choose more than one answer. In the study group, there were significantly more male physicians (p=0.0140) and those working in the industry (p=0.0308), while there were significantly more female pharmacists than male (p=0.0482). It is noteworthy that in the study group almost half of the respondents (49.8%) are involved in the creation of NMVO. Demographic data is summarized in Table 1. From the perspective of the country of origin, respondents were mostly representatives of Belgium (10.7%), Poland (7.9%), UK (7.9%), Czech Republic (7.1%) and Romania (7.5%) as shown in Table 2.

https://doi.org/10.18549/PharmPract.2017.04.1031

Table 2. Distribution of respondents by country.

| Country | Response in percent |
|---|---|
| Austria | 4.4% |
| Belgium | 10.7% |
| Bulgaria | 2.8% |
| Croatia | 2.0% |
| Cyprus | 1.2% |
| Czech Republic | 7.1% |
| Denmark | 0.8% |
| Estonia | 1.6% |
| Finland | 2.0% |
| France | 0.8% |
| Germany | 4.8% |
| Greece | 2.8% |
| Hungary | 5.2% |
| Ireland | 5.6% |
| Italy | 2.4% |
| Latvia | 0.8% |
| Lithuania | 0.4% |
| Luxembourg | 1.2% |
| Malta | 1.6% |
| Netherlands | 2.0% |
| Norway | 0.8% |
| Poland | 7.9% |
| Portugal | 5.6% |
| Romania | 7.5% |
| Slovakia | 0.4% |
| Slovenia | 1.6% |
| Spain | 4.0% |
| Sweden | 4.4% |
| United Kingdom | 7.9% |

In the study group, 95.7% of people have heard about FMD, while only 4.3% of the respondents have not heard about FMD thus far. In the study group, there were significantly more respondents who have heard about the provisions of the FMD (p=0.0001). Younger respondents and those with lower levels of education rarely have heard about this EU regulation (respectively, p=0.0014, p=0.0001). Physicians have less frequently heard about the FMD as compared to pharmacists (p=0.0063), people working in the industry (p=0.0014), and respondents with a different professional profile (p=0.0114). In the study group, 89.6% of people were aware of the NMVO role in the process of implementing the provisions of FMD into the national system of medicinal product distribution, while 10.4% of the respondents responded negatively. There were significantly more respondents aware of the role of NMVO (p=0.0001). Again, younger respondents (p=0.0027) and those characterized by a lower level of education (p=0.0186) were less likely to be aware of the role of NMVO in the process of implementing changes on the national level. Pharmacists and professionals related to the pharmaceutical industry are significantly more likely to understand the role of NMVO in the implementation of FMD (p=0.0001). There were significantly more respondents in the study population who knew the deadline for implementation of FMD i.e. 91.9% (p=0.0001), but both younger respondents and those with lower levels of education were less aware of the timing requirements that national regulators have to satisfy (p=0.0003, p=0.0023). In addition, respondents were aware of the need to choose a provider of medicinal product authentication, which is one of the basic requirements faced by those responsible for implementing new EU regulations at the national level. Only 10.4% of respondents were not aware of this obligation. There are significantly more people who were aware of this problem (89.6%, p=0.0001). It should also be noted that in the study group, 79.1% of the respondents realized that the verification of medicinal products must comply with the standards and guidelines (Blueprint) for the country as defined by EMVO (p=0.0001). However, respondents with a medical education understood the need to implement the FMD significantly less when compared to pharmacists (p=0.0064) and people working in the industry (p=0.0001). No statistically significant differences were seen in the distribution of responses between men and women. Objective data is summarized in Table 3.

Table 3. Characteristics of respondents in terms of the study objective.

| **Have you heard of the Falsified Medicines Directive? (n=252)** | | | |
|---|---|---|---|
| | **Men (n=153)** | **Women (n=99)** | **p-value** |
| Yes | 130 (95.6%) | 72 (96.0%) | 0.8873 |
| No | 6 (4.4%) | 3 (4.0%) | |
| Age | **Yes** | **No** | |
| 21-29 | 3 (1.5%) | 2 (22.2%) | 0.0014 |
| 30-39 | 26 (12.9%) | 2 (22.2%) | |
| 40-49 | 72 (35.6%) | 1 (11.1%) | |
| 50-59 | 73 (36.1%) | 3 (33.3%) | |
| 60 and more | 28 (13.9%) | 1 (11.1%) | |
| Education | **Yes** | **No** | |
| Primary education | 1 (0.5%) | 1 (11.1%) | 0.0001 |
| The level of single structure education | 0 (0.0%) | 1 (11.1%) | |
| General secondary education | 5 (2.5%) | 0 (0.0%) | |
| Secondary vocational education | 5 (2.5%) | 0 (0.0%) | |
| Post-secondary non-tertiary education | 17 (8.4%) | 1 (11.1%) | |
| Tertiary education | 174 (86.1%) | 6 (66.7%) | |
| Profession | **Yes** | **No** | |
| Physician | 5 (71.4%) | 2 (28.6%) | |
| Pharmacist | 96 (96.0%) | 4 (4.0%) | |
| Employed in the industry | 57 (98.3%) | 1 (1.7%) | |
| Other specialties | 53 (96.4%) | 2 (3.6%) | |

https://doi.org/10.18549/PharmPract.2017.04.1031

Table 3 (cont.). Characteristics of respondents in terms of the study objective.

| | | | |
|---|---|---|---|
| **Are you aware of the role of a NMVO? (n=252)** | | | |
| | **Men (n=153)** | **Women (n=99)** | **p-value** |
| Yes | 123 (90.4%) | 66 (88.0%) | 0.5786 |
| No | 13 (9.6%) | 9 (12.0%) | |
| Age | **Yes** | **No** | |
| 21-29 | 2 (1.1%) | 3 (13.6%) | 0.0027 |
| 30-39 | 25 (13.2%) | 3 (13.6%) | |
| 40-49 | 68 (36.0%) | 5 (22.7%) | |
| 50-59 | 66 (34.9%) | 10 (45.5%) | |
| 60 and more | 28 (14.8%) | 1 (4.5%) | |
| Education | **Yes** | **No** | |
| Primary education | 1 (0.5%) | 1 (4.5%) | 0.0186 |
| The level of single structure education | 0 (0.0%) | 1 (4.5%) | |
| General secondary education | 5 (2.6%) | 0 (0.0%) | |
| Secondary vocational education | 5 (2.6%) | 0 (0.0%) | |
| Post-secondary non-tertiary education | 17 (9.0%) | 1 (4.5%) | |
| Tertiary education | 161 (85.2%) | 19 (86.4%) | |
| Profession | **Yes** | **No** | |
| Physician | 2 (28.6%) | 5 (71.4%) | |
| Pharmacist | 91 (91.0%) | 9 (9.0%) | |
| Employed in the industry | 55 (94.8%) | 3 (5.2%) | |
| Other specialties | 50 (90.9%) | 5 (9.1%) | |
| **Do you understand that there is a deadline for implementation of the FMD? (n=252)** | | | |
| | **Men (n=153)** | **Women (n=99)** | |
| Yes | 126 (92.6%) | 68 (90.7%) | 0.6129 |
| No | 10 (7.4%) | 7 (9.3%) | |
| Age | **Yes** | **No** | |
| 21-29 | 2 (1.0%) | 3 (17.6%) | 0.0003 |
| 30-39 | 25 (12.9%) | 3 (17.6%) | |
| 40-49 | 67 (34.5%) | 6 (35.3%) | |
| 50-59 | 71 (36.6%) | 5 (29.4%) | |
| 60 and more | 29 (14.9%) | 0 (0.0%) | |
| Education | **Yes** | **No** | |
| Primary education | 1 (0.5%) | 1 (5.9%) | 0.0023 |
| The level of single structure education | 0 (0.0%) | 1 (5.9%) | |
| General secondary education | 5 (2.6%) | 0 (0.0%) | |
| Secondary vocational education | 5 (2.6%) | 0 (0.0%) | |
| Post-secondary non-tertiary education | 18 (9.3%) | 0 (0.0%) | |
| Tertiary education | 165 (85.1%) | 15 (88.2%) | |
| Profession | **Yes** | **No** | |
| Physician | 3 (42.9%) | 4 (57.1%) | |
| Pharmacist | 94 (94.0%) | 6 (6.0%) | |
| Employed in the industry | 54 (93.1%) | 4 (6.9%) | |
| Other specialties | 52 (94.5%) | 3 (5.5%) | |
| **Are you aware that according to the introduced directive the NMVO must select a medicines authentication service provider to establish a repository system in your country? (n=252)** | | | |
| | **Men (n=153)** | **Women (n=99)** | **p-value** |
| Yes | 125 (91.9%) | 64 (85.3%) | 0.1345 |
| No | 11 (8.1%) | 11 (14.7%) | |
| Age | **Yes** | **No** | |
| 21-29 | 2 (1.1%) | 3 (13.6%) | 0.0018 |
| 30-39 | 24 (12.7%) | 4 (18.2%) | |
| 40-49 | 65 (34.4%) | 8 (36.4%) | |
| 50-59 | 69 (36.5%) | 7 (31.8%) | |
| 60 and more | 29 (15.3%) | 0 (0.0%) | |
| Education | **Yes** | **No** | |
| Primary education | 1 (0.5%) | 1 (4.5%) | 0.0190 |
| The level of single structure education | 0 (0.0%) | 1 (4.5%) | |
| General secondary education | 5 (2.6%) | 0 (0.0%) | |
| Secondary vocational education | 4 (2.1%) | 1 (4.5%) | |
| Post-secondary non-tertiary education | 17 (9.0%) | 1 (4.5%) | |
| Tertiary education | 165 (85.1%) | 15 (88.2%) | |
| Profession | **Yes** | **No** | |
| Physician | 2 (28.6%) | 5 (71.4%) | |
| Pharmacist | 90 (90.0%) | 10 (10.0%) | |
| Employed in the industry | 54 (93.1%) | 4 (6.9%) | |
| Other specialties | 52 (94.5%) | 3 (5.5%) | |

| Table 3 (cont.). Characteristics of respondents in terms of the study objective. | | | |
|---|---|---|---|
| **Do you know that in order to provide a medicines authentication service you should select a EMVO selected blueprint provider? (n=252)** | | | |
| | **Men (n=153)** | **Women (n=99)** | **p-value** |
| Yes | 112 (82.4%) | 55 (73.3%) | 0.1227 |
| No | 24 (17.6%) | 20 (26.7%) | |
| Age | **Yes** | **No** | |
| 21-29 | 2 (1.2%) | 3 (6.8%) | 0.0012 |
| 30-39 | 21 (12.6%) | 7 (15.9%) | |
| 40-49 | 50 (29.9%) | 23 (52.3%) | |
| 50-59 | 66 (39.5%) | 10 (22.7%) | |
| 60 and more | 28 (16.8%) | 1 (2.3%) | |
| Education | **Yes** | **No** | |
| Primary education | 1 (0.6%) | 1 (2.3%) | 0.2865 |
| The level of single structure education | 0 (0.0%) | 1 (2.3%) | |
| General secondary education | 3 (1.8%) | 2 (4.5%) | |
| Secondary vocational education | 4 (2.4%) | 1 (2.3%) | |
| Post-secondary non-tertiary education | 15 (9.0%) | 3 (6.8%) | |
| Tertiary education | 144 (86.2%) | 36 (81.8%) | |
| Profession | **Yes** | **No** | |
| Physician | 2 (28.6%) | 5 (71.4%) | |
| Pharmacist | 76 (76.0%) | 24 (24.0%) | |
| Employed in the industry | 51 (87.9%) | 7 (12.1%) | |
| Other specialties | 47 (85.5%) | 8 (14.5%) | |

## DISCUSSION

Our study aimed to explore the European Economic Area (EEA) pharmaceutical companies professionals' awareness of the implementation of the FMD. Those surveyed will be directly responsible for the changes in the marketing supply chain of medicinal products, the production of drugs (the area of industrial activity), as well as wholesale and retail (public and hospital pharmacies). Our study has clearly shown that the awareness of the legal regulations related to FMD among pharmaceutical company professionals, is high but not sufficient enough. In this context, it is worth emphasizing the fact that over 10% of the respondents are not aware of what the FMD is. In addition, those who are less aware are people with a lower level of education, those who are younger and those in the medical profession (physicians). It seems important to note that pharmacists are more aware of the consequences of FMD implementation.

The organization of both the European and national data repositories will require close cooperation of the participating parties.[20] Hamilton *et al*. indicates that these actions should focus on multi-faceted interventions; initially, based on the certification of medicinal products and secondarily, on the effective prosecution of pharmaceutical crimes and a strong, partnership of all the parties.[4] In this regard, the awareness of the respondents seems insufficient. As suggested by Naughton *et al*., it is necessary to implement Good Authentication Practice (GAP), a collection of standards and procedures aimed at improving the process of verification of medicinal products, particularly in the stage of the flow of medicines between the pharmaceutical wholesalers and the community pharmacies.[21] The introduction of such procedures could significantly improve awareness of the provisions related to the new EU regulations. While such actions are only theoretical at this point, they must be considered the next step in the process of shaping legislation in the area of authentication procedures. In this context, once again it is worth emphasizing the topicality and innovation of our study, as it is the awareness of the decision-makers that will determine the efficiency of the process. Until now, awareness of the dangers of falsified medicines has been studied primarily in the context of the distribution of medications in illegal places, i.e. bazaars, gyms or purchased over the Internet, especially in relation to sexual potency drugs and anabolic steroids. One study showed that 90% of physicians, 80% of nursing staff, but only 40% of people not connected to the health sector were aware of the risks associated with the pandemic of falsified medications produced in Ukraine or China.[22] Despite this, awareness of the procedures necessary for verification of a medication's authenticity among health care workers should be considered highly insufficient.[23] While the risk of falsification is disproportionately smaller in the case of legally purchased or hospital dispensed medicines, it is the healthcare professionals who should have an increased awareness and vigilance of the potential risk of falsification.[24] In this context, the results of our survey should be considered important, as they show that knowledge of the procedures related to the implementation of anti-falsifying regulations is small among doctors professionally linked to regulatory affairs and pharmacovigilance.

This study is an important voice in the discussion about implementing the Falsified Medicines Directive to the European system of medicine distribution. It seems necessary to introduce the solutions of the authorities of the Community to popularize this knowledge among Member States pharmaceutical company representatives. Important communication tools could be conferences on an international scale, as well as European associations of representatives of innovative or generics pharmaceutical companies, organizations of pharmaceutical wholesalers or pharmaceutical lines of work. A huge responsibility rests also on the people responsible for shaping drug policy, both at a central and national level. Our study should be regarded as useful for European decision-makers. As there is little time remaining before countries of the European Union must implement these new legislations, remaining months should be spent in intensified efforts. The pharmaceutical company representatives' awareness of the

financial consequences of the regulations remains an open question. Although awareness of financial responsibility was not part of the aim of this study, it could be a preliminary start for future research projects. It should be highlighted that implementation of FMD should be considered as a starting point for deeper collaboration among stakeholders. For instance, thanks to these new regulations, the system of monitoring of adverse events should improve the collection of safety alerts. However, these amendments will necessitate excellent cooperation among stakeholders involved in drug distribution and require detailed procedures.[25] Moreover, as suggested by Naughton *et al.*, current technology needs further improvement before there can be harmonization with the current workflow in community and hospital pharmacies.[26]

Our study can lead to some practical implications. First of all, the intensification of efforts to popularize knowledge about the fight against falsified medicines in the legal supply chain among people responsible for the implementation of FMD guidelines in the Member States of the European Community should be undertaken. A special beneficiary of such actions will be individuals with a medical education, younger and those with lower levels of education. From a scientific point of view, further representative studies are needed to achieve a higher generality. Secondly, we could consider collecting data from one selected stakeholder, for instance from a wholesaler, which could provide a more insightful perspective. Moreover, to investigate more subtle barriers and to find an explanation as to why some parts of FMD legislation are less known, qualitative studies could be considered useful. Above all, highly effective communication between stakeholders involved in the implementation of FMD is necessary to improve knowledge and the understanding of the barriers which hinder the harmonization.

**Limitations**

Our study also has some limitations. Firstly, the major limitation is the 17% response rate and thus our findings cannot be considered as the public opinion in EEA. However, during the study, we intensified our effort to collect responses from a wide range of participants and used various sources of contact details. Secondly, is the fact that only contact details that were available on the Internet were used in the study. As such, the questionnaires did not reach representatives of pharmaceutical companies whose data is not publicly available and/or was not collected during conferences or business meetings by members of the research team. Moreover, most of the questions included in our questionnaire are general, and we did not provide detailed issues, e.g. deadlines. This was done purposefully, as some of the countries may have their own arrangements and schedules, with the individual Member States being in various stages of implementation of EU regulations hence the executives' professionals' awareness may vary. Finally, the questionnaire was provided in an English language version which for most of our respondents is not their first language (L1). However, for individuals working in pharmaceutical industry, a high level of English proficiency is usually required.[27] It should be emphasized, however, that the authors have made efforts to objectify the research process.

## CONCLUSIONS

Bearing in mind the limitations of our study, particularly the limited number of respondents, we can still declare that awareness of the regulations related to the implementation of FMD among pharmaceutical companies' professionals in the EU, although relatively high, is still insufficient. Further educational initiatives and research are warranted.

**ACKNOWLEDGEMENTS**

We would like to thank Bio Stat for the statistical study of the test results and Roksana Zgierska MA and Natalia Cwalina MD for their assistance during the preparation of this manuscript. The authors also would like to thank Dr. David A Brindley of Oxford University for his help in designing the questionnaire used in the study. We thank Graham Smith and Mark De Simone from Aegate Ltd for their contribution and support during the preparation of our paper. We express our sincere appreciation and thanks to the following organizations for providing their help and guidance at each stage of our research: the Royal Pharmaceutical Society (UK), Polish National Pharmaceutical Chamber (Poland) and the Polish Pharmaceutical Society (Poland). We also thank Regis Vaillancourt (pharmacy director), at Children's Hospital of Eastern Ontario (CHEO) Pharmacy, Canada for his expertise and pointing out the most important aspects from the perspective of the International Pharmacy Federation (FIP).

## CONFLICT OF INTEREST

It must be emphasized that this publication was created purely for scientific practice and academic interest and must not be construed in any way as an investment recommendation. Piotr Merks is a research assistant at the Department of Pharmaceutical Technology, Faculty of Pharmacy, Ludwig Rydygier Collegium Medicum in Bydgoszcz and was an employee of Aegate Ltd in Poland (2015-2017).

## FUNDING

None.

## References

1. WHO. Substandard and Falsified (SF) Medical Products. Available at: http://www.who.int/medicines/regulation/ssffc/en/ (accessed 23rd August 2017).
2. Kaur H, Clarke S, Lalani M, Phanouvong S, Guérin P, McLoughlin A, Wilson BK, Deats M, Plançon A, Hopkins H, Miranda D, Schellenberg D. Fake anti-malarials: start with the facts. Malar J. 2016;15:86. doi: 10.1186/s12936-016-1096-x

3. Intellectual Property Watch. WHO Group Suggests New Name For Falsified Medicines, Dropping 'Counterfeit'. Available at: https://www.ip-watch.org/2016/11/28/group-suggests-new-name-falsified-medicines-dropping-counterfeit/ (accessed on 23 August 2017).
4. Hamilton WL, Doyle C, Halliwell-Ewen M, Lambert G. Public health interventions to protect against falsified medicines: a systematic review of international, national and local policies. Health Policy Plan. 2016;31(10):1448-1466. doi:10.1093/heapol/czw062
5. European Medicines Agency. Falsified medicines. Available at: http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000186.jsp (accessed on 23 August 2017).
6. Nayyar GM, Attaran A, Clark JP, Culzoni MJ, Fernandez FM, Herrington JE, Kendall M, Newton PN, Breman JG. Responding to the pandemic of falsified medicines. Am J Trop Med Hyg. 2015;92(6 Suppl):113-118. doi:10.4269/ajtmh.14-0393
7. Pharmaceutical crime. A major threat to public health. Available at: https://www.interpol.int/Crime-areas/Pharmaceutical-crime/Pharmaceutical-crime (accessed on 18 May 2017).
8. Buckley GJ, Gostin LO, eds. Countering the Problem of Falsified and Substandard Drugs. Washington (DC): National Academies Press; 2013. ISBN: 978-0-309-26939-1.
9. Price R. EAHP President Joan Peppard advises members to heighten their awareness of the Falsified Medicines Directive in 2016. Eur J Hosp Pharm Sci Pract. 2016;23(2):124. doi:10.1136/ejhpharm-2016-000910
10. Price R. EU: Falsified medicines directive "Delegated act" accepted by European parliament. Eur J Hosp Pharm Sci Pract. 2016;23(3):183-186. doi:10.1136/ejhpharm-2016-000954
11. Commission Delegated Regulation (EU) 2016/161 of 2 October 2015 supplementing Directive 2001/83/EC of the European Parliament and of the Council by laying down detailed rules for the safety features appearing on the packaging of medicinal products for human use. Official Journal of the European Union. Available at: https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2016_161/reg_2016_161_en.pdf (accessed on 23 August 2017).
12. Directive 2011/62/EU of the European Parliament and of the Council of 8 June 2011 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products. Official Journal of the European Union. Available at: https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/dir_2011_62/dir_2011_62_en.pdf (accessed on 23 August 2017).
13. Qadri S. The current status and implementation of the Falsified Medicines Directive in the EU. Regulatory Rapporteur. 2014;11(5):11-15.
14. Sinclair-Jenkins B, Andrews R, Rees I. The falsified medicines directive: A regulatory perspective. Regulatory Rapporteur. 2014;11(5):5-7.
15. Merks P, Swieczkowski D, Byliniak M, Drozd M, Krupa K, Jaguszewski M, Brindley DA, Naughton BD. The European Falsified Medicines Directive in Poland: background, implementation and potential recommendations for pharmacists. Eur J Hosp Pharm Sci Pract. 2016 [Ahead of print]. doi:10.1136/ejhpharm-2016-000970
16. MHRA. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/339997/consultation_FMD_safety_features_listing.pdf (accessed on18 May 2017).
17. Price R. Falsified Medicines Directive news: EDQM announce collaboration with the European Medicines Verification Organisation. Eur J Hosp Pharm Sci Pract. 2016;23(1):61. doi:10.1136/ejhpharm-2015-000851
18. New rules to help fight falsified medicines. Available at: https://www.gov.uk/government/news/new-rules-to-help-fight-falsified-medicines (acesed on 18 May 2017).
19. European Union sets February 2019 for serialized authentication of pharma products. Available at: http://pharmaceuticalcommerce.com/information-technology/european-union-sets-february-2019-for-serialized-authentication-of-pharma-products/ (acesed on 18 May 2017).
20. Smith G, Smith JA, Brindley DA. The Falsified Medicines Directive: How to secure your supply chain. J Generic Med. 2014 Sep;11(3-4):169-172. doi:10.1177/1741134315588986
21. Naughton BD, Smith JA, Brindley DA. Establishing good authentication practice (GAP) in secondary care to protect against falsified medicines and improve patient safety. Eur J Hosp Pharm Sci Pract. 2016;23(2):118-120. doi:10.1136/ejhpharm-2015-000750
22. Binkowska-Bury M, Wolan M, Januszewicz P, Mazur A, Fijalek ZE. What Polish hospital healthcare workers and lay persons know about counterfeit medicine products? Cent Eur J Public Health. 2012;20(4):276-281.
23. Binkowska-Bury M, Januszewicz P, Wolan M, Sobolewski M, Krauze M, Fijalek ZE. Counterfeit medicines in Poland: opinions of primary healthcare physicians, nurses and lay persons. J Clin Nurs. 2013;22(3-4):559-568. doi:10.1111/j.1365-2702.2012.04166.x
24. Jackson G, Patel S, Khan S. Assessing the problem of counterfeit medications in the United Kingdom. Int J Clin Pract. 2012;66(3):241-250. doi:10.1111/j.1742-1241.2011.02826.x
25. Beninger P. Opportunities for collaboration at the interface of pharmacovigilance and manufacturing. Clin Ther. 2017;39(4):702-712. doi: 10.1016/j.clinthera.2017.03.010
26. Naughton B, Roberts L, Dopson S, Chapman S, Brindley D. Effectiveness of medicines authentication technology to detect counterfeit, recalled and expired medicines: a two-stage quantitative secondary care study. BMJ Open. 2016;6(12):e013837. doi: 10.1136/bmjopen-2016-013837
27. EF English Proficiency Index for Companies. Available at: https://www.ef.com/__/~/media/centralefcom/epi/v4/downloads/epi-c/ef-epi-c-English-191114.pdf (accessed 24 August 2017).