The Effect of Covid-19 and Brexit on Compliance of the Falsified Medicines Directive

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This dissertation is dedicated to my parents, Ivan and Elvie,
for all their love and support

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Abstract

The Falsified Medicines Directive (FMD) was ratified in July 2011. The motivation behind the FMD is to stop falsified drugs from reaching patients.

The aim of this study was to evaluate the impact of Brexit and Covid-19 on compliance with the FMD.

Three questionnaires were disseminated to pharmacists, two in Malta pre and post-unique identifier (UI) implementation and one in Bonn post-UI implementation. A focus group discussing the consequences of Brexit and Covid-19 with respect to the FMD was conducted and the results were analysed.

Eighty-five participants answered the pre-implementation questionnaire in Malta. Participants never encountered a case of falsified drugs (n=78), agree that the UI will increase their workload (n=56), cause drug prices to increase (n=46), will decrease entry of falsified medicines in the legal supply chain (n=69), and is worth its financial impact (n=34). Seventeen participants answered the post-implementation questionnaire in Bonn and eighty-six participants answered the post-implementation questionnaire in Malta. Participants never encountered a case of falsified drugs (Bonn: n=15; Malta: n=72), agree that that the UI caused an increase in their workload (Bonn: n=12; Malta: n=56), caused drug prices to increase (Bonn: n=0; Malta: n=23), has decreased entry of falsified drugs in the legal supply chain (Bonn: n=9; Malta: n= 48) and is worth its financial impact (Bonn: n=3; Malta: n=29).

Brexit related challenges identified during the focus group included Malta's historical dependence on the UK market, its small market, and the current lack of Maltese importers able to affix the safety features to medicinal packs. With respect to Covid-19, strengths identified included the temporary exemption granted by the EU to

manufacturers of the Covid-19 vaccines from having to bear the safety features. Weaknesses identified included the high demand for Covid-19 vaccines and other medications being used for Covid-19.

The UI is seen as effectively preventing falsified drugs, but most participants did not agree that it is worth its financial impact. Increase in workload was envisaged and experienced by pharmacists surveyed. Brexit and Covid-19 present a challenge to pharmaceutical stakeholders, which is further complicated by the implementation of FMD.

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List of Abbreviations

ABPI: The Association for British Pharmaceutical Industry

API Active Pharmaceutical Ingredient

CPSU Central Procurement and Supplies Unit

EAEPC European Association of Euro-Pharmaceutical Companies

EC European Commission

EFPIA European Federation of Pharmaceutical Industries and Associations

EMVO European Medicines Verification Organization

EMVS European Medicines Verification System

EU European Union

EUIPO European Union Intellectual Property Office

FREC Faculty Research Ethics Committee

GIRP European Healthcare Distribution Organization

GTIN Global Trade Identification Number

MA Marketing Authorization

MaMVO Malta Medicines Verification Organization

MaMVS	Malta Medicines Verification System
MMA	Malta Medicines Authority
NHS	National Health Service
NMVO	National Medicines Verification Organization
NMVS	National Medicines Verification System
ODT	Operational Dispensing Time
PGEU	Pharmaceutical Group of the European Union
PreIQ	Pre-Implementation Questionnaire
PostIQB	Post-Implementation Questionnaire Bonn
PostIQM	Post-Implementation Questionnaire Malta
SME	Small and Medium Enterprises
UI	Unique Identifier
WHO	World Health Organization

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Chapter 1

Introduction

1.1 Background

The prevalence of falsified medicines is an issue that continues to present a challenge to countries around the world.[1] The Falsified Medicines Directive (Directive 2011/62/EU) defines a falsified medicinal product as:[2]

"*Any medicinal product with a false representation of:*

> *(a) Its identity, including its packaging and labeling, its name or its composition as regards any of the ingredients including excipients and the strength of those ingredients;*
>
> *(b) Its source, including its manufacturer, its country of manufacturing, its country of origin or its marketing authorization holder; or*
>
> *(c) Its history, including the records and documents relating to the distribution channels used."*

The Directive then goes on to add to the above definition that medicinal products of a substandard quality where this is accidental are not to be considered as falsified

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[1] European Medicines Agency (EMA). Falsified Medicines [Internet]. London: EMA; 2020 [cited 2021 Aug 29]. Available from:

[2] European Commission. 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 [Internet]. Official Journal of the European Union. 2011; L174:74-87 [cited 2021 Aug 29]. Available from: https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:174:0074:0087:EN:PDF

medicines. The same applies in any case where there is infringement of intellectual property rights.[2]

According to the European Medicines Agency (EMA), up until not long ago, incidents of falsified medicines penetrating the supply chain of prosperous countries involved costly medicines.[1]

Instances of falsified medicines entering the supply chain are becoming more common.[1] The aim of Directive 2011/62/EU is to decrease the risk of falsified medicines entering the supply chain, by requiring certain drugs to bear an anti-tampering device and a Unique Identifier.[1]

1.2 The Impact of Falsified Medicines

The risk of falsified medicines gaining entry into the legal supply chain as a result of poor supply chain management, increase in the demand for medicinal products and the growing emergence of e-commerce, is on the increase.[3] Falsified medicines also pose a threat to the health of the one taking them due to these products usually being lacking in quality, safety and efficacy.[3]

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[2] European Commission. 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 [Internet]. Official Journal of the European Union. 2011; L174:74-87 [cited 2021 Aug 29]. Available from: https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:174:0074:0087:EN:PDF

[1] European Medicines Agency (EMA). Falsified Medicines [Internet]. London: EMA; 2020 [cited 2021 Aug 29]. Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000186.jsp&mid=WC0b01ac058002d4e8

[3] World Health Organization (WHO). A Study on the Public Health and Socioeconomic Impact of Substandard and Falsified Medicinal Products [Internet]. Geneva: WHO; 2017 [cited 2021 Aug 29]. Available from: https://www.who.int/medicines/regulation/ssffc/publications/Layout-SEstudy-WEB.pdf

1.2.1 Falsified Medicines and the Legal Supply Chain

Falsified medicines can get into the supply chain at multiple instances.[4] In an impact assessment report released by the European Commission in 2008, manufacturers stated that their products might pass through approximately twenty different pairs of hands before being sold at a community/hospital pharmacy, making the legal supply chain very complex (Figure 1.1).[4] This increases the probability of the entry of falsified drugs into the supply chain since each transaction can be seen as having a potential for infiltration by falsified medicines (Liu & Lundin, 2016).

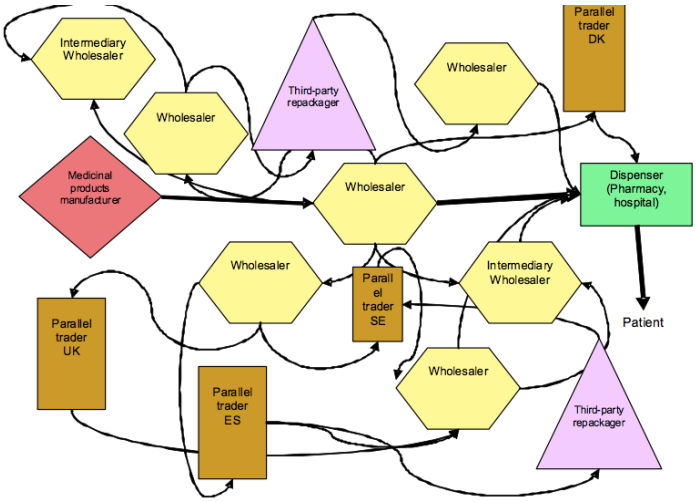

Fig. 1.1: The legal supply chain

Figure reproduced from: European Commission (EC). Accompanying document to the proposal for a directive of the European Parliament and of the council amending directive 2001/83/EC as regards the prevention of the entry into the legal supply chain of medicinal products which are falsified in relation to their identity, history or source [Internet]. Brussels: EC; 2008 [cited 2021 Aug 29]. Available from: https://ec.europa.eu/health//sites/health/files/files/pharmacos/pharmpack_12_2008/counterfeit-ia_en.pdf

[4] European Commission (EC). Accompanying document to the proposal for a directive of the European Parliament and of the council amending directive 2001/83/EC as regards the prevention of the entry into the legal supply chain of medicinal products which are falsified in relation to their identity, history or source [Internet]. Brussels: EC; 2008 [cited 2021 Aug 29]. Available from: https://ec.europa.eu/health//sites/health/files/files/pharmacos/pharmpack_12_2008/counterfeit-ia_en.pdf

For example, in the USA a case was recorded in which falsified Epoetin Alfa was purchased from a pharmacy. In this case the product had passed through 13 different pairs of hands before being dispensed to the patient (Blackstone et al., 2014). Apart from the manufacturer and a wholesaler the Epoetin Alfa was also in the possession of 3 other wholesalers, 4 unauthorized intermediaries, 2 pharmacies, and 1 suspected counterfeiter (Blackstone et al., 2014). What this case illustrates is that decreasing the complexity of the supply chain can help curb the entry of falsified medicines into the supply chain and in turn improve the safety of consumers (Blackstone et al., 2014).

In another case in the USA it was found that a batch of Avastin®, an anti-cancer drug, contained no active ingredient (Mackey et al., 2015). Another study stated that there were 11 known cases of falsified medicines in the UK between 2001 and 2011 and 222 known instances of substandard medicines during these 10 years (Almuzaini et al., 2013).

For years, rising amounts of falsified medication have been encountered in European countries, maybe as a result of the increasingly global nature of the legal supply chain (Karev & Raychev, 2019).

It is also worth noting that under-reporting of incidents of falsified medicines is a problem that limits our understanding of the situation (Ghanem, 2019). Reporting of events related to falsified medicines usually occurs after the occurrence of a major incident, but this has created a literature gap since a significant amount of incidents are unreported and therefore remain unaccounted for (Ghanem, 2019).

The multinational nature of markets is also putting the integrity of the supply chain at risk (Liu & Lundin, 2016). A study by Barrett (2019) also states that parallel importation in Europe allows for drugs to be transported along the supply chain over vast geographical areas, therefore making the supply chain susceptible to infiltration by falsified medicines.

According to Thomas (2019), supply chain risk and security has had five steps in its evolution (Figure 1.2), these being:

Stage 1 Reactive approach to security and risk problems.
Stage 2 Risk and security are controlled using specialized methods e.g. track and trace/ serialisation.
Stage 3 Supply chain security and risk are at an operationally excellent level
Stage 4 Supply chain security and risk are established as basic prerequisites in all processes from the patient to the business and all parts of supply.
Stage 5 Risk and security capabilities are established all around the ecosystem and network both internal and external to a company; Integrity and availability of products along with patient safety are taken as fact.

Figure 1.2 Evolution of Supply Chain Risk and Security

Figure adapted from: Thomas F. Supply Chain Risk and Security Maturity Evolution. Pharmaceutical Technology. 2019;43(6):45.

1.2.2 Falsified Medicines and Public Health

According to the World Health Organization (WHO) falsified medicines pose a significant threat to public health because these products may contain the incorrect amount of active pharmaceutical ingredient (API), the wrong API, or expired ingredients.[5] This in turn may result in under or over dosage or intake of dangerous substances. In the best-case scenario this may have no effect on the patient, but in the worst-case scenario this may worsen the condition of the individual and cause adverse drug reactions.[5] Falsified medicines also result in a loss of money for patients who will be buying a product that will not have any beneficial outcomes (Blackstone et al., 2014). Confidence in the safety of medicines may also decrease among patients, which may lead to a decrease in adherence (Blackstone et al., 2014; Johnston & Holt, 2014). It should be noted that the problem of falsified medicines is not solely present in developing countries, despite how it is estimated that in developed countries with adequate regulation and market control the percentage of falsified medicines sold is less than 1% (Johnston & Holt, 2014; Karev & Raychev, 2019).

An incident in 2012 involved the falsification of Bevacizumab in the USA, where the API was replaced with salt and starch (Blackstone et al., 2014). Another incident in the USA involved the replacement of Heparin with a cheaper version of this API, causing patients to have adverse drug reactions and causing a worldwide recall of Heparin (Blackstone et al., 2014). The conditions in which the medications are manufactured and transported may also not abide by the principles of good practice, which may lead to the ingredient degradation and reduction in the overall quality of the product.[5]

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[5] World Health Organization (WHO). Substandard and falsified medical products [Internet]. Geneva: WHO; 2018 [cited 2021 Aug 29]. Available from: http://www.who.int/mediacentre/factsheets/fs275/en/

One of the main impacts of falsified medicines is the proliferation of anti-microbial resistance due to the use of sub therapeutic doses in substandard medicines (Johnston & Holt, 2014). In this way falsified medicines contribute towards the spread of infections such as Malaria, Tuberculosis and HIV (Johnston & Holt, 2014). Moreover, the therapeutic failure of substandard narrow spectrum antibiotics may lead to the use of broad-spectrum antibiotics, which further contributes to the spread of resistance (Johnston & Holt, 2014; Ghanem, 2019).

1.3 The Unique Identifier and the Anti-Tampering Device

The EU passed the Falsified Medicines Directive (FMD) - Directive 2011/62/EU to combat the threats presented by falsified medicines. This directive amends a previous directive (Directive 2001/83/EC), which regulates medicinal products for human use.[1] Two of the main measures introduced in the FMD are the Unique Identifier (UI) and the Anti-Tampering Device (ATD).[1] Commission Delegated Regulation (EU) 2016/161 which supplements Directive 2001/33/EC, defines the UI as:[6]

"The safety feature enabling the verification of the authenticity and the identification of an individual pack of a medicinal product"

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[1] European Medicines Agency (EMA). Falsified Medicines [Internet]. London: EMA; 2020 [cited 2021 Aug 29]. Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000186.jsp&mid=WC0b01ac058002d4e8

[6] European Commission. 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 [Internet]. Official Journal of the European Union. 2016; L32:1-27 [cited 2021 Aug 29]. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0161&from=EN

The idea behind the UI is that once a product is released from the manufacturing site the manufacturer activates the UI of the respective products.[6] Once the product reaches the end of the supply chain the UI is deactivated by the dispensing pharmacist to guarantee that the product is genuine.[6]

Commission Delegated Regulation (EU) 2016/161 defines the ATD as:[6]

"The safety feature allowing the verification of whether the packaging of a medicinal product has been tampered with"

Before a medicinal pack is dispensed to a patient the dispensing pharmacist must check the ATD for any signs of damage.[6] If the ATD is damaged this could be a sign that the pack has been tampered with and should therefore be set aside and not dispensed.[6]

1.3.1 Properties of the UI

Commission Delegated Regulation 2016/161, which was adopted on the 2nd of October 2015, and which supplements Directive 2001/83/EC, provides details regarding the presentation of the safety features, including the UI, on the packaging of drug products.[6]

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[6] European Commission. 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 [Internet]. Official Journal of the European Union. 2016; L32:1-27 [cited 2021 Aug 29]. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0161&from=EN

Commission Delegated Regulation 2016/161 lays out the technical specifications of the UI. These are:[6]

- The UI should consist of a sequence of numbers or a combination of letters and numbers
- The data elements that make up the UI should be as follows:
    - A code that can be used to identify certain properties of the product (ex. Trade and Generic names, formulation, pack size etc.)
    - A randomly generated sequence of numbers only or letters and numbers (not more than 20 characters) – The serial number
    - The batch number and expiry date
    - The national reimbursement number (optional)
- The UI should be encoded in a 2-D Data matrix barcode
- The barcode should be on a smooth and low-reflecting surface on the medicinal pack

Commission Delegated Regulation 2016/161 also states that the likelihood of the UI being guessed should be lower than 0.01%.[6] It should also be noted that the sequence of characters in the UI of a particular pack cannot be reused for one year minimum after the product's expiry date, or for five years minimum after the dispensing of the pack.[6] The product code, serial number and national reimbursement number shall be in human-readable format, but this does not apply if when the lengths of the two

[6] European Commission. 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 [Internet]. Official Journal of the European Union. 2016; L32:1-27 [cited 2021 Aug 29]. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0161&from=EN

largest dimensions of a pack are added the resultant number is less or equal to 10 cm.[6] If the printing quality of the UI is of 1.5 (complying with ISO/IEC 15415:2011) or more this is presumed to be in compliance with the requirements.[6]

1.3.2 Activation, Verification and Deactivation of UI

The manufacturer should undertake activation of the UI once the product is released for sale. Commission Delegated Regulation 2016/161 states that manufacturers, wholesalers and those responsible for dispensing medicinal products to the public should check the authenticity of the UI by making sure that the repositories system contains an active UI which has the same product code and serial number as the UI being verified.[6]

The decommissioning of a UI should be made by the person with the authorization to supply the public with medicinal products, at the time of dispensing.[6] An exception to this is that in a healthcare institution it is acceptable for the person authorized to supply the public with medicinal products to verify and decommission the UI at an earlier stage (i.e. not at the time of dispensing of the product).[6] In preliminary research by Naughton et al. (2015) it was found that verification and decommissioning of the UI just before dispensing is the best option. Nevertheless, another study by Naughton (2017) states that at least in the beginning, the added step of decommissioning will no doubt have a negative effect on the dispensing process in UK and EU pharmacies. Another disadvantage associated with decommissioning the UI at the point of

[6] European Commission. 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 [Internet]. Official Journal of the European Union. 2016; L32:1-27 [cited 2021 Aug 29]. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0161&from=EN

dispensing is that if the product is found to not be authentic and no replacement product is available this may cause inconvenience to the patient (Naughton, 2017). In a study set in a National Health Service (NHS) hospital in the UK, it was found that the average response times for decommissioning/verification/re-commissioning/ duplicating scans of each medicinal pack was 131ms, which is well within the maximum time of 300ms set by the EU (Naughton. 2019). Naughton (2019) also found that there were a number of incidents due to offline errors and 37 cases of packs being quarantined incorrectly out of the 2188 packs having the UI. Out of these 37 cases of incorrect quarantine it was observed that 17 of these cases occurred during an offline period. It was also found that during offline periods pharmacy staff were cautious and tended to quarantine products. The staff were also observed to use a pen to mark the UI as authenticated in cases the pack was opened and partially dispensed (Naughton, 2019).

Commission Delegated Regulation 2016/161 states that the decommissioning of a UI can be reversed only if:[6]

- The person reverting the status of the UI back to active must be authorized to supply medicinal products to the public, as well as work in the same premises as the person who decommissioned the UI;
- A decommissioned UI cannot have its status reverted back to active after ten days from its decommissioning;

[6] European Commission. 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 [Internet]. Official Journal of the European Union. 2016; L32:1-27 [cited 2021 Aug 29]. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0161&from=EN

- The product is still within its expiry date and it has been neither recalled, withdrawn, stolen or intended for destruction.

Wholesalers are entitled to decommission a UI in certain circumstances, which are listed Commission Delegated Regulation 2016/161. These are:[6]

- Products meant for distribution outside the EU
- Products that have been returned to the wholesaler and cannot be resold
- Products that are going to be destroyed
- Products that are requested from the wholesaler by competent authorities as a free sample
- Products that the wholesaler intends to distribute to the list of persons and institutions referred to in Article 23 of the same delegated regulation.

Naughton et al. (2015) state that preferably only full packs should be dispensed, but in the event that a pack needs to be split, the original container should only leave the premises once all of the contents have been dispensed, allowing for verification of the pack every time some of its contents are dispensed. Commission Delegated Regulation 2016/161 states that in the case of only part of a pack being dispensed, the UI on that pack should be verified and decommissioned the first time that the pack is opened.[6]

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[6] European Commission. 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 [Internet]. Official Journal of the European Union. 2016; L32:1-27 [cited 2021 Aug 29]. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0161&from=EN

Commission Delegated Regulation 2016/161 also says that the persons with the authorization to provide medicines to the public also have an obligation to decommission the UI when:[6]

- They are in possession of medicinal products that cannot be returned to a wholesaler;
- Giving out a sample to a competent authority;
- Medicinal products dispensed are to be used as authorized investigational medicinal products or authorized auxiliary medicinal products.

1.4 Implementation of the Falsified Medicines Directive

The rules laid down in the delegated regulation 2016/161 started being enforced on the 9th of February 2019 by all member states except Italy and Greece, who had the option to postpone the implementation of these rules by up to six years.[7] Belgium also had the option to delay the implementation of the UI, but they decided to start applying these rules by the 9th of February 2019.[7]

Commission Delegated Regulation 2016/161 states that the UI itself shall be present on the packaging for prescription only medicines (POM), but not on that for over the counter (OTC) drugs.[6] KPMG issued an advisory report on the implementation of the

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[7] European Commission (EC). Safety features for medicinal products for human use questions and answers - Version 18 [Internet]. Brussels: EC; 2021 [cited 2021 Aug 15]. Available from: https://ec.europa.eu/health/sites/health/files/files/falsified_medicines/qa_safetyfeature_en.pdf

[6] European Commission. 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 [Internet]. Official Journal of the European Union. 2016; L32:1-27 [cited 2021 Aug 15]. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0161&from=EN

FMD, and stated that the rules on the UI should also apply to OTC drugs since OTC drugs may have the same APIs as POM drugs. The OTC supply chain is less regulated than the POM supply chain, therefore making the former more vulnerable to falsification.[8]

Commission Delegated Regulation 2016/161 establishes the process for transition into the new system and states that medicinal products lacking the UI, which are already distributed at the time that the FMD becomes applicable, may be sold or distributed until their expiry date.[6]

In a study carried out in community pharmacies in England, 39.2% of participants reported not being ready for the implementation of the FMD (Barrett, 2020), while another study by Franco and Gouveia (2020) which was carried out in an oncology institute in Lisbon, Portugal, found that six months after the implementation of the FMD only around 69% of products bear a UI.

Part of the implementation of Directive 2011/62/EU included the setup of a repositories system.[6]

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[8] KPMG. Advice on the Implementation of EU-Directive 2011/62/EU [Internet]. Amstelveen: KPMG; 2013 [cited 2021 Aug 29]. Available from: http://www.producencilekow.pl/wp-content/uploads/2017/11/raport_kpmg.pdf

[6] European Commission. 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 [Internet]. Official Journal of the European Union. 2016; L32:1-27 [cited 2021 Aug 29]. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0161&from=EN

1.5 Properties of the Repositories System

The repositories system stores information on the unique identifiers. Commission Delegated Regulation 2016/161 states that this repositories system is to be established and maintained by non-profit legal entities subject to the manufacturers and MAH's of the products bearing the UI.[6] According to the study by Merks et al. (2016), non-profit legal entities in Poland did not have much influence in the implementation of a national repository system regardless of European legislation.

The repositories system is made up of a central/European hub and repositories that either serve one member state (National Repository) or more than one member state (Supranational Repository). [6]

Each EU member state also created a National Medicines Verification Organization (NMVO) whose task it is to select a verification provider from the two companies available, these being Arvato Systems GmbH and Solidsoft Reply (Naughton, 2017). The chosen verification provider works with the NMVO in order to deploy the National Medicines Verification System (NMVS) that serves to facilitate authentication of medicines, as well as to provide a blueprint system based on the requirements of the FMD (Naughton, 2017).

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[6] European Commission. 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 [Internet]. Official Journal of the European Union. 2016; L32:1-27 [cited 2021 Aug 29]. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0161&from=EN

Commission Delegated Regulation 2016/161 states that data uploaded to the repositories system for each individual product containing the UI, should include at least:[6]

- The data elements of the unique identifier;
- The generic and trade names of the product, along with the dose, dosage form, pack type and pack size;
- Name and address of manufacturing company responsible for including the safety features on the package as well as those of the MAH;
- The code that identifies the entry equivalent to the product bearing the medicinal product in the database referred to in Article 57(1)(l) of Regulation (EC) No 726/2004 of the European Parliament and the Council;
- The wholesalers that are listed by the MAH as the ones storing and distributing the medicinal products included in the MA in the name of the MAH;

Commission Delegated Regulation 2016/161 lists that the functions of the repositories system with respect to the UI are as follows:[6]

- Verifying that active UIs are authentic;
- Sending out an alert should a UI be proved to be inauthentic;
- Decommissioning of active UIs and reversing this in certain circumstances;

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[6] European Commission. 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 [Internet]. Official Journal of the European Union. 2016; L32:1-27 [cited 2021 Aug 29]. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0161&from=EN

- Providing information about the UI of a particular product when requested by EMA or national competent authorities;

The Maltese NMVO, the Malta Medicines Verification Organization (MaMVO), is made up of 3 full member organizations, these being The Pharmaceutical Research Based Industry Malta Association (PRIMA), The Malta Chamber of SME's (GRTU) and the Malta Chamber of Pharmacists.[9] Apart from these, two other organizations have signed on as associate members, these being the Central Procurement and Supplies Unit (CPSU) and the Malta Qualified Persons Association.[9]

MaMVO had the option of choosing either of two options to set up an NMVS. These were to either join a supranational repository or else to set up an NMVS specific to Malta. An NMVS specific to Malta (MaMVS) was set up and Solidsoft Reply was eventually chosen to be the blueprint provider.[10]

1.6 Course of Action when Falsification is suspected

If it is suspected that a medicinal pack is falsified, it is the responsibility of the manufacturer/wholesaler/person authorized to dispense medicinal products to the public, to inform the national competent authority.[6] The procedures used to inform

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[9] Malta Medicines Verification Organization (MaMVO). About Us [Internet]. Valletta: MaMVO; 2020 [cited 2021 Aug 29]. Available from: https://www.mamvo.org/about/

[10] Malta Medicines Verification Organization (MaMVO). IT Suppliers [Internet]. Valletta: MaMVO; 2020 [cited 2021 Aug 29]. Available from: https://www.mamvo.org/on-boarding/itsuppliers/

[6] European Commission. 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 [Internet]. Official Journal of the European Union. 2016; L32:1-27 [cited 2021 Aug 29]. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0161&from=EN

the national competent authority on a suspected falsified medicinal product should be decided on by the individual member states.[7] Moreover, Article 46 of Directive 2001/83/EC states that manufacturers have a duty to inform the market authorization holder of the medicinal product which is suspected to be falsified.[7]

1.7 Impact of the UI on Stakeholders

The FMD and the introduction of the UI represent a significant development for stakeholders such as pharmacists, wholesale dealers and pharmaceutical manufacturers throughout the EU, and will also have an impact on the NHS and regulatory agencies (Kermani, 2015).

1.7.1 Financial Impact

According to Kermani (2015) manufacturers will need to invest money in order to implement Directive 2011/62/EU. It is estimated that tamper-evidence measures will account for 47% of the total cost of implementation of this directive, 37% of the total cost will be due to the implementation of serialisation, and 16% of this cost will be devoted to authentication (Kermani, 2015).

It was made clear by the European Commission that no financial aid will be given to manufacturers to mitigate the costs of implementing these measures.[7]

In a joint response by the European Association of Euro-Pharmaceutical Companies

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[7] European Commission (EC). Safety features for medicinal products for human use questions and answers - Version 18 [Internet]. Brussels: EC; 2021 [cited 2021 Aug 29]. Available from: https://ec.europa.eu/health/sites/health/files/files/falsified_medicines/qa_safetyfeature_en.pdf

(EAEPC), European Federation of Pharmaceutical Industries and Associates (EFPIA), European Healthcare Distribution Association (GIRP) and the Pharmaceutical Group of European Union (PGEU), to a concept paper on the detailed rules for a UI for medicinal products for human use, which was released for public consultation, these organizations estimate that the costs for adapting packaging lines will be approximately €0.16 per pack (this figure covers the cost in a whole year).[11]

The purchase of a 2D scanner by pharmacies will amount to about €250-€300 and the software extension required in pharmacies will amount to €0-€4000 per pharmacy.[11] On the other hand GIRP estimates that costs for scanners for wholesalers will amount to approximately €1200 (the increased cost being due to additional requirements for wholesale dealers).[11] The cost of the European Medicines Verification System (EMVS) is estimated to amount to €120,000,000 to €205,000,000 per year throughout the EU.[11]

While the costs estimated above are substantial, it is important to note that the potential savings due to the implementation of the directive will mitigate these costs.[12] Among these is that the introduction of the UI will lead to a decrease in the number of falsified medicines entering the supply chain, and this in turn will lead to an increase in sales of legitimate medicinal products, and therefore increased profits for the stakeholders.[12]

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[11] EAEPC, EFPIA, GIRP, PGEU. Coding and Serialization [Internet]. 2012 [cited 2021 Aug 29]. Available from: https://ec.europa.eu/health/sites/health/files/files/falsified_medicines/2012-06_safety-features/efpia-eaepc-girp-pgeu_en.pdf

[12] European Commission (EC). Impact assessment accompanying the document Commission Delegated Regulation (EU) no .../... 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 [Internet]. Brussles: EC; 2015 [cited 2021 Aug 29]. Available from: http://ec.europa.eu/smart-regulation/impact/ia_carried_out/docs/ia_2015/swd_2015_0189_en.pdf

A study by Naughton (2017) posits that fake medicines cost the industry €10.2 billion per annum. This figure is supported in a report by the European Union Intellectual Property Office (EUIPO), which also estimates that the legal supply chain loses approximately €10.2 billion per annum due to falsified medicines, corresponding to around 4.4% of sales, and that 37,700 jobs are lost as a direct result of the lost sales due to falsified medicines.[13] In Malta, the legal supply chain also loses around €6 million due to falsified medicines.[13] A study by Fittler et al. (2020) carried out in Hungarian hospital pharmacies found that a mean of €1868 per institution was spent on non-human resources after February 2019 (high inter-institution cost was also observed due to the difference in scale between different institutions). It was also noted that in the long-term, expenses are expected to be much lower compared to the initial phase (Fittler et al., 2020).

In a study carried out in community pharmacies in England, only a small percentage of pharmacists reported increased profitability for community pharmacies as a result of the implementation of the FMD (Barrett, 2020). For small and medium enterprises (SMEs) the financial impact of the implementation of the safety measures will be larger than it is for larger companies.

The cost of setting up the NMVO is to be covered by the MAHs.[6] In Malta the adjusted

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[13] European Union Intellectual Property Office (EUIPO). The economic cost of IPR infringement in the pharmaceutical industry [Internet]. Alicante: EUIPO; 2016 [cited 2021 Aug 29]. Available from: https://euipo.europa.eu/tunnel-web/secure/webdav/guest/document_library/observatory/resources/research-and-studies/ip_infringement/study9/pharmaceutical_sector_en.pdf

[6] European Commission. 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 [Internet]. Official Journal of the European Union. 2016; L32:1-27 [cited 2021 Aug 29]. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0161&from=EN

flat fee model has been adopted to pay for this, more specifically the Marketing Authorization (MA) based model.[14] Authorization Holders in Malta are split into two groups: those uploading products into MaMVS (Group A) and Article 126(A) and Parallel Importers (Group B).[14] The former pay a flat fee rate of €9000 in annual fees per authorization holder, while the latter pay a fee in accordance to the number of licenses in their possession.[14]

1.7.2 Impact on Access to Medicines

According to a study by Milmo (2018), there was a possibility that the implementation of the UI would result in a shortage of medicinal products throughout the EU. This was because of companies that did not meet the deadline for implementation of the safety features (9th February 2019).

In a study by Van Baelen (2017), it is posited that increasing cost due to the falsified medicines directive may also contribute to drug shortages, especially for generic medicines, whose industry is more susceptible to economic changes and cost-containment measures. Nevertheless, since the implementation of the FMD, the retail price of 29 medications in Malta decreased in 2019.[15]

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[14] Malta Medicines Verification Organization (MaMVO). Marketing Authorisation Holders [Internet]. Valletta: MaMVO; 2021 [cited 2021 Aug 29]. Available from: https://wx2.830.myftpupload.com/on-boarding/mahs2021/

[15] Malta Medicines Authority (MMA). Annual Report 2019 [Internet]. San Gwann: MMA; 2019 [cited 2021 Aug 29]. Available from: http://www.medicinesauthority.gov.mt/file.aspx?f=4705

A study by Miceli and Serracino-Inglott (2018) found that the wholesale dealers who are not representing the MAH are impacted, due to complications with the new supply chain. It was postulated that this may cause delays in the delivery of medicinal products to pharmacies and patients.

1.7.3 Impact on Work Load and Dispensing Time

Pinto de et al. (2017) studies the impact of the implementation of the Falsified Medicines Directive on dispensing time in an Austrian hospital. Results showed that operational dispensing time (ODT) in an environment where the Falsified Medicines Directive was implemented increased by 81% when compared to an environment where normal dispensing operations were carried out, with the respective ODTs for eighty orders being 10 hours for the former and 5.62 hours for the latter. It was also observed that for the hospital to cope with the workload associated with the introduction of the UI, 3.5 full-time employees will need to be hired. The study than goes on to suggest that automation will help to reduce the impact that the UI will have on ODT as this will decrease the number of staff that will need to be hired as a direct result of the implementation of Directive 2011/62/EU.

In a study by Franco and Gouveia (2020), the average time to read a UI code was found to be 9.5s. This included connecting to the software, verification of the safety device, scanning of the barcode and waiting for the result of the scan. This study concluded that the time required to scan the UI amounted to 29 working hours in 8 working days. On the other hand, a study by Merks et al. (2020) in a hospital pharmacy in Poland

found that the average time taken for the verification or decommissioning of a medicinal pack was 3.05s. A study by Fittler et al. (2020) found that the average increase in pharmacist workload after the implementation of the FMD was of 0.92 hours/day. It was also estimated that pharmacist workload would increase by a further 1.13 hours/day, amounting to 0.25 pharmacist full time equivalents per institution. This study also found a significant increase in the workload of pharmacy technicians after the implementation of the FMD (Fittler et al., 2020).

A study carried out in community pharmacies in England showed that the majority of participants felt that their workload had increased as a result of the introduction of the UI (Barrett, 2020).

1.7.4 Impact on Parallel Trade

Parallel Traders are designated as manufacturers in the Falsified Medicines Directive and as such are required to augment packaging and IT systems.[16] Parallel Traders are also required to contribute to the costs of the EMVS.[17] Increased regulation on parallel traders due to the Falsified Medicines Directive may also be of benefit to trademark owners and their licensees.[16] If a parallel trader repackages a product in order to comply with the specifications of the MA in the market it will be sold in, and in the process removes its UI, the parallel trader is obliged to replace the UI with an equivalent one that obeys all of the specifications laid out by Delegated Regulation

[16] Havard R, Barrett-Major J. EU: Falsified Medicines Directive: Implications for parallel importers and of Brexit [Internet]. London: AA Thornton; 2018 [cited 2021 Aug 29]. Available from: https://www.aathornton.com/eu-falsified-medicines-directive-implications-for-parallel-importers-and-of-brexit/

[17] Krähenbühl C. EU-Falsified Medicines Directive EMVO and NMVO – Stakeholder Awareness Meeting. Presentation; 2017; Malta.

2016/161 and the removed UI will have to be decommissioned and the new UI will have to be uploaded onto the national repository.[7]

1.7.5 Impact of the Unique Identifier on Hospital Pharmacies

Naughton (2017) asserts that hospital pharmacies face a more complicated situation compared to community pharmacies. Naughton (2017) also asserts that the biggest difference between the application of the Falsified Medicines Directive in community and hospital pharmacies is the point at which the UI is decommissioned.

Commission Delegated Regulation 2016/161 is clear that in community pharmacies, decommissioning is to take place at the point of dispensing. In contrast, hospital pharmacies are given the option of decommissioning the UI before the point at which the product is dispensed to the patient.[6]

Naughton (2017) goes on to note that if hospitals take the option to deactivate the UI as soon as the product is received from the supplier this may require the employment of staff to specifically carry out this task. Naughton (2017) also notes that If ten days elapse from the time that the UI is decommissioned at the hospital, the product cannot be sold to another organization since the UI cannot be reactivated after ten days of its decommissioning. This would limit the profit made by hospitals that also act as wholesale dealers. Another study by Naughton et al. (2016) shows that staff whose

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[7] European Commission (EC). Safety features for medicinal products for human use questions and answers - Version 18 [Internet]. Brussels: EC; 2021 [cited 2021 Aug 29]. Available from: https://ec.europa.eu/health/sites/health/files/files/falsified_medicines/qa_safetyfeature_en.pdf

[6] European Commission. 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 [Internet]. Official Journal of the European Union. 2016; L32:1-27 [cited 2021 Aug 29]. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0161&from=EN

responsibility it is to check prescriptions are more likely to adhere to the process of authentication of medicines than the dispensing staff, making this a reasonable stage at which decommissioning should be considered.

Another point of consideration is that in hospitals medicines are not always dispensed from the pharmacy directly to the patient but can be dispensed to other hospital staff such as nurses and porters. This further complicates the process (Naughton, 2017). In a study by Burri & Scheidegger (2019), five Swiss hospitals were asked to rate the acceptability of different options for the decommissioning of dispensed medicinal packs. All five hospitals rated the option to decommission upon arrival at the hospital as 'ok', three hospitals were capable of decommissioning dispensed medicinal packs as they were leaving the pharmacy, and two hospitals were capable of decommissioning dispensed medicinal packs upon arriving at the ward.

1.8 Challenges Associated with the UI

Smith et al. (2015) identifies a number of challenges in introducing the falsified medicines directive. Due to the fact that the safety features are only applicable to prescription only medicines, this might cause problems should a previously over the counter medicine's status be changed to prescription only. Another aspect of this is that different medicines have different classifications in different member states; this means that, depending on the country, manufacturers and re-packagers (e.g. parallel traders) will have to include the UI on the packaging in accordance to where the product will be sold.[8]

[8] KPMG. Advice on the Implementation of EU-Directive 2011/62/EU [Internet]. Amstelveen: KPMG; 2013 [cited 2021 Aug 29]. Available from: http://www.producencilekow.pl/wp-content/uploads/2017/11/raport_kpmg.pdf

Another problem is code-harvesting, i.e. the collection of active UIs by criminals intending to use them on fake medicines.[8] In certain situations it may be the case that a medicinal product bearing the safety features is dispensed without the UI being decommissioned. Case in point being if a particular dispensary/wholesaler has failed to establish a functioning system for authentication within their pharmacy by the 9th of February 2019.[8] In this case the UIs on the dispensed products will still remain active and therefore can be used by falsifiers to make their fake product seem authentic.[8]

In a number of EU member states there is broadband coverage of less than 80%, and in some areas no Internet connection is available at all.[8] This may lead to problems when connecting to the repositories system, which in turn may lead to a code-harvesting problem.[8] Another observation is that the gathering of data in in the repositories systems could lead to serious consequences should there be a breach in the system security, leading to theft of data by counterfeiters as well as others.[8]

A study by Naughton (2017) concludes that unfortunately not much was made by way of preparation from the hospital/community pharmacy end in the immediate years following the publication of Directive 2011/62/EU. The same study also makes reference to the huge task that had to be undertaken by the National Medicines Verification Organizations (NMVO) in loading serialized drug codes into the national medicines verification databases, as well as making certain that the technology required to communicate with dispensaries and wholesalers throughout the EU is in place before the February deadline.

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[8] KPMG. Advice on the Implementation of EU-Directive 2011/62/EU [Internet]. Amstelveen: KPMG; 2013 [cited 2021 Aug 29]. Available from: http://www.producencilekow.pl/wp-content/uploads/2017/11/raport_kpmg.pdf

A study by Cayeux et al. (2019) showed that one of the major problems encountered during decommissioning of the UI was legibility of the 2D barcode. A total of 107 products from 23 providers (representing 8.5% of products from the study) presented with this problem. According to this study, the problem in this case was always due to the 2D barcode being printed on a black background.

In a study carried out in an oncology institute in Lisbon, Portugal, it resulted that 12.9% of packages (N=10,935 packages) bearing the UI had at least one problem with the scanning of the UI (Franco & Gouveia, 2020).

A number of difficulties specific to Malta were identified in the setting up of the NMVS.[18] These included:[18]

- Approximately half of products by volume in Malta are registered with article 126a. This poses a problem since products registered under this article are usually not meant specifically for the Maltese market, and therefore the relevant information required to verify and decommission these packs would not be available in the NMVS, leading to an inter-market query;
- Lack of Economies of Scale;
- Lack of IMS Data, which complicates the processes of data collection and analysis;
- Products on the Maltese market are usually imported from other countries and all these need to be recorded in the NMVS. This could result in a situation

[18] Falzon N. MaMVO. Workshop on EU Falsified Medicines Directive. Presentation; 2017; Malta.

where Malta would have one of the largest repositories in the EU, notwithstanding it being one of the smallest countries;

1.9 The Impact of Brexit on the Falsified Medicines Directive

On the 31st of January of 2020 the United Kingdom ceased to be a member state of the EU.[19] This had far reaching consequences on the pharmaceutical industry in both the UK and the EU (Batraga et al., 2020), including on the implementation of the Falsified Medicines Directive. After Brexit, UK pharmacies and wholesalers are no longer legally obliged to carry out verification and decommissioning of UIs, and UK stakeholders also lost connection to the UK NMVS.[20] This also brings up concerns of falsified medicines being able to penetrate the UK supply chain (Kazzazi et al., 2017).

In Malta this is of particular concern due to the Maltese market being historically dependent on the UK market.[21] Before Brexit, Malta was highly dependent on Article 126a authorizations, which allow for medicines licensed in another EU country to be placed on the Maltese market without a marketing authorization (Musazzi et al., 2020), with 63.8% of all 126a authorisations being connected to licenses in the UK.[21] After Brexit, those 126a authorizations connected to a marketing authorization in the UK became invalid.[22]

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19 European Commission (EC). The New Normal [Internet].Brussels: EC; 2021 [cited 2021 Aug 29]. Available from: https://ec.europa.eu/info/relations-united-kingdom/new-normal_en

20 The Association of British Pharmaceutical Industry (ABPI). How will Brexit affect the FMD and its' processes? [Internet]. London: ABPI; 2021[cited 2021 Aug 29]. Available from: https://www.abpi.org.uk/new-medicines/supply-chain/falsified-medicines-directive-fmd/faqs-on-fmd-and-dr-for-pharmaceutical-manufacturers/how-will-brexit-affect-the-fmd-and-its-processes/

21 Farrugia C. Preparations for the impact of Brexit on the pharmaceutical supply chain in Malta [Internet]. Milan: Pharma World; 2018 [cited 2021 Aug 29]. Available from: https://www.pharmaworldmagazine.com/preparations-for-impact-of-brexit-pharmaceutical-supply-chain-malta/

22 Malta Medicines Authority (MMA). Authorisation in line with regulation 4(2) of the Medicines (Marketing Authorisation) Regulations, in accordance with article 126(a) of Directive 2001/83/EC [Internet]. Malta: MMA; 2021 [cited 2021 Aug 29]. Available from: http://medicinesauthority.gov.mt/126a

1.10 The Impact of Covid-19 on the Falsified Medicines Directive

The risk of counterfeited products increased during the Covid-19 pandemic due to the high demand for products that are being used against the Covid-19 virus (Newton & Bond, 2020; Tesfaye et al., 2020). This is further exacerbated due to the chaos caused in global supply chains as a result of Covid-19 (Newton & Bond, 2020). Kohler and Mackey (2020) also highlight the urgency required to ensure worldwide access to medicines used in the Covid-19 pandemic, as well as the importance of protecting Covid-19 vaccines from falsification. In order to ensure a faster distribution of Covid-19 vaccines, EU countries agreed to use one Global Trade Item Number (GTIN) in the UI printed on Covid-19 vaccine packaging.[23] A study by Forcinio (2021) reports that in a survey conducted by the International Data Corporation, 75% of companies stated that Covid-19 increases risk of falsification of essential products like vaccines and antiviral drugs. Cases of falsified Chloroquine in Cameroon and the Democratic Republic of Congo (Gnegel et al., 2020), and defective personal protective equipment and Covid-19 testing kits have been reported (Erku et al., 2021). The EMA has warned against buying medicines online from non-licensed sellers due to increased counterfeiting during the Covid-19 pandemic.[24] As primary healthcare providers, pharmacists have a role in limiting the spread of misinformation relating to the Covid-19 pandemic, as well as mitigating the risk of falsified medicines reaching patients (Erku et al., 2021).

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[23] European Medicines Agency (EMA). Questions and Answers on Labeling Flexibilities for Covid-19 Vaccines [Internet] Netherlands: EMA; 2021 [cited 2021 Aug 29]. Available from: https://www.ema.europa.eu/en/documents/other/questions-answers-labelling-flexibilities-covid-19-vaccines_en.pdf

[24] European Medicines Agency (EMA). Covid-19: Beware of falsified medicines from unregistered websites [Internet]. Netherlands: EMA; 2020 [cited 2021 Aug 29]. Available from: https://www.ema.europa.eu/en/news/covid-19-beware-falsified-medicines-unregistered-websites

1.11 Aims and Objectives

The aims of this study are:

1) To compare the envisaged impact of the UI with the actual impact of the UI as experienced by pharmacists in Malta before and after the Falsified Medicines Directive is enforced.
2) To compare the impact of the UI as experienced by pharmacists in Malta and in Bonn, Germany after the Falsified Medicines Directive is enforced.
3) To assess the impact of Brexit and the Covid-19 pandemic on compliance with the Falsified Medicines Directive.

These aims will be carried out by:

- Using validated questionnaires, which will be distributed among pharmacists working in different pharmaceutical sectors (e.g. community pharmacy, industrial pharmacy, etc.), before and after the UI is introduced in Malta and after the UI is introduced in Bonn.
- Convening a focus group made up of pharmacists working in different pharmaceutical sectors to discuss the impact of Brexit and Covid-19 on the Falsified Medicines Directive.

Chapter 2

Methodology

2.1 Study Setting

The main interest of this cross-sectional study was the comparison between the envisaged impact of the unique identifier (UI) and the actual impact of the UI according to pharmacists working in Malta, as well as the study of the impact of the Covid-19 pandemic and Brexit on compliance with and implementation of the FMD. To this end, pharmacists working in different sectors (including community pharmacy, hospital pharmacy, regulatory sciences, wholesale dealing and industrial pharmacy) were surveyed using convenience sampling, both before and after the introduction of the UI. Community pharmacists working in Bonn, Germany, were also surveyed via convenience sampling regarding the impact of the UI after its introduction.

A focus group comprising of seven pharmacists from different pharmaceutical sectors was then convened to discuss the impact of the Covid-19 pandemic and Brexit on the FMD.

2.2 Ethics Approval

Ethics approval was obtained from the University of Malta Faculty Research Ethics Committee (FREC) before data collection was carried out

2.3 Questionnaire Design and Development

Three anonymous, self-administered questionnaires each made up of two sections, were developed in the English language. One questionnaire was to be disseminated to pharmacists in Malta before the implementation of the UI (Pre-Implementation Questionnaire - PreIQ), one questionnaire was to be disseminated to pharmacists in Malta after the implementation of the UI (Post-Implementation Questionnaire – Malta -

PostIQM) and the third was to be disseminated to pharmacists working in Bonn after the implementation of the UI (Post-Implementation Questionnaire – Bonn - PostIQB).

A number of literary sources were used, including peer-reviewed journals, reports and websites, in order to identify the areas relevant to the pharmaceutical profession that might be impacted as a result of the introduction of the UI.

In November 2018, a focus group was conducted with the participation of five pharmacists from different work backgrounds. These included a community pharmacist, a hospital pharmacist, a pharmacist working in regulatory sciences, a responsible person working within a wholesale dealership and a pharmacist working within the pharmaceutical industry. A consent form was given to the participants, informing them of their rights and assuring them that everything would be confidential. This was read and signed before the start of the discussion. The topics discussed during this focus group included falsified medicines in the EU, the UI's ability to curb the problem of falsified medicines in the EU, the amount of information available to pharmacists and patients regarding the UI, the level of preparedness for the introduction of the UI, the financial impact of the UI, and the impact of the UI on access to medicines, workload and drug prices. Using the points put forward during this focus group together with knowledge obtained by analyzing the literature, the PreIQ was developed.

Since a comparison was to be made between the PreIQ and the post-implementation questionnaires, the differences between these questionnaires are minimal. The changes made to the PreIQ to develop the post-implementation questionnaires were:

i. Changes in verb tense from future tense to past/present tense to reflect that the UI had been introduced.

ii. Removal of an explanation for the phrase ‘decommissioning of the UI’ since it was assumed that after the implementation of the UI all participants would be aware of the meaning of this phrase.

iii. Addition of an open-ended question to allow for participants to add any other comments.

Differences between the PostIQM and the PostIQB included:

i. Changes in questions asking specifically about Malta, with them now referring to Germany/EU instead.

ii. Change in the options presented for a question asking when the participant heard about the UI, to reflect that dissemination of the post-implementation questionnaire in Bonn was done in 2019 and dissemination of the post-implementation questionnaire in Malta is being done in 2020.

2.4 Structure of Questionnaires

Each questionnaire was divided into two sections. The first section consisted of questions regarding demographic data and the second section consisted of questions regarding falsified medicines and the unique identifier. In all three questionnaires the first section contained six questions. In the pre-implementation questionnaire the second section contained ten questions while in the post-implementation questionnaire this section contained eleven questions.

2.4.1 Section 1: Demographic Data

According to Vogt and Johnson (2015) demography is a discipline where the variables describing a particular group of people who are studied. The importance of collecting demographic data lies in the fact that it gives the ability to the researcher to characterize a subset of the population at a specific point in time (Connelly, 2013). The first section of the questionnaires collected the demographic data of participants including age, gender, work sector, years of experience, and job position. With respect to work sector, participants were asked to choose between community pharmacy, hospital pharmacy, industrial pharmacy, wholesale dealing, regulatory sciences and other. This section was identical in all three questionnaires.

2.4.2 Section 2: Falsified Medicines and the Unique Identifier

In all three questionnaires, the second section consisted of a question regarding encounters with falsified medicines and eight questions assessing knowledge, perception and impact of the UI, which consisted of both close-ended and open-ended questions. A five-point Likert scale question, with 1 corresponding to strongly disagree and 5 corresponding to strongly agree, consisting of sixteen close-ended statements relating to the UI and falsified medicines was also included. The Likert scale is a psychometric tool in which participants give scores to different items and as a result allow the researcher to quantify their views on any number of subjects (Bishop and Herron, 2015).

In both post-implementation questionnaires, an open-ended question was added to allow participants to add any comments they may wish to share.

Close-ended questions were preferred over open-ended ones, since the former are much easier and quicker for participants to answer with, as well as making it easier for

the researcher to conduct statistical analysis and comparison. A major disadvantage of close-ended questions is that any misunderstanding or inattention on the part of the participant may go unnoticed by the researcher.

2.5 Questionnaire Validation

The pre-implementation questionnaire (PreIQ) was sent to five pharmacists for face and content validation in early January 2019. Face validity is the extent to which the questionnaire appears to measure what it is intended to measure (Garcia et al., 2009), while content validity is the extent to which the questionnaire covers all the aspects of the topic being researched (Garcia et al., 2009). Two community pharmacists, a responsible person, a hospital pharmacist, and a pharmacist working in regulatory sciences were asked to validate the questionnaire. These pharmacists were asked to give their opinions regarding the clarity, relevance and completeness of the questions asked in the questionnaire. They were also asked to mention whether any questions should be added or removed from the questionnaire.

Since there are only very small differences present between the pre-implementation questionnaire and the post-implementation questionnaires (to allow for proper comparison between the results obtained pre-implementation and post-implementation), results obtained from the validation of the PreIQ were considered to also hold true for the post-implementation questionnaires.

2.6 Questionnaire Dissemination

Dissemination for all three questionnaires was done via convenience sampling. Convenience sampling is a type of non-probability and non-random sampling technique whereby members of the population being studied are recruited to participate in the study based on them being conveniently available to participate (Etikan, 2016). A number of advantages are associated with this technique (Etikan, 2016), including:

- The simplicity and ease of the technique;
- It is cheaper compared to alternative sampling techniques;

Convenience sampling also has a number of disadvantages, namely the vulnerability to selection bias and outliers (Etikan, 2016).

2.6.1 Dissemination of the PreIQ

The PreIQ was disseminated to pharmacists working in Malta in January and early February 2019. Dissemination of the PreIQ was conducted by sharing the questionnaire on a social media platform for pharmacists. Six out of the eight community pharmacies invited to take part in the study agreed to participate.

2.6.2 Dissemination of the PostIQB

The PostIQB was disseminated to pharmacists working in Bonn, Germany, throughout November and December 2019. Dissemination of this questionnaire was done in thirteen community pharmacies (pharmacists in thirty-seven community pharmacies were originally invited to participate).

2.6.3 Dissemination of the PostIQM

The PostIQM was disseminated to pharmacists working in Malta, starting February 2020 till March 2021. Dissemination of the PostIQM was done by sharing the questionnaire on a social media platform for pharmacists and sharing the questionnaire with individual pharmacists using convenience sampling.

2.6.4 Statistical Analysis of Questionnaires

Statistical analysis of the questionnaires was carried out using SPSS version 27. The Chi Squared test and the Mann-Whitney test were used during the statistical analysis of the questionnaire results.

These tests were used to compare the views of local participants before and after the introduction of the UI. They were also used to compare the views of participants in Malta and Bonn after the introduction of the UI. In this case the null hypothesis specifies that there is no significant differences between the two groups and is accepted if the p-value exceeds the 0.05 level of significance. The alternative hypothesis specifies that there is a significant difference between the two groups and is accepted if the p-value is less than the 0.05 criterion.

2.7 Focus Group

In January 2021, a focus group was convened with the participation of seven pharmacists from different backgrounds, including regulatory sciences (n=2), wholesale dealing (n=1), the Central Procurement and Supplies Unit (CPSU) (n=1), industrial pharmacy (n=1), and MaMVO (n=2). The impact of the Covid-19 pandemic and Brexit on the FMD in Malta, as well as the challenges associated with implementation of the FMD, and the risk of falsified medicines penetrating the supply chain, were discussed. The points put forward during the focus group were then analysed.

Chapter 3

Results

In this chapter, questionnaire validation results, questionnaire participant demographics, knowledge of the UI, preparedness for the implementation of the UI, and views on the financial impact of the UI, impact of the UI on workload, and impact of the UI on access to medicines, are presented. The views expressed by focus group participants on the impact of Brexit and the Covid-19 pandemic on the FMD are also presented.

3.1 Questionnaire Validation Results

Table 3.1 shows the changes that were implemented to the questionnaire as suggested by the five pharmacists who carried out questionnaire validation.

Changes Made to Pre-Implementation Questionnaire (PreIQ)	
Addition of Question	Have you ever encountered Falsified medication during your practice?
	Malta's dependence on 126(a) products, parallel trade products and small and medium enterprises means that it has been hit harder with respect to accessibility to medicines than other EU countries?
Change in Question	Addition of ‘per week’ to ‘If yes, how many more man-hours will be required per week?’

Table 3.1: Changes made to PreIQ after questionnaire validation

3.2 Questionnaire Participant Characteristics

A total of eighty-five pharmacists answered the PreIQ. From these participants, thirty-six were male and forty-nine were female. The mean age of these participants was thirty-eight years and ranged from twenty-four to sixty-eight years of age. Thirty-two participants had 1-10 years of experience, twenty-one had 11–20, twenty-six had 21–30, and six had over 30 years of experience. Thirty-one participants were hospital pharmacists, twenty-six participants were community pharmacists, nine participants worked in wholesale dealing, seven participants worked in regulatory science, four participants were industrial pharmacists, and eight participants listed another pharmaceutical sector – these included medical representation (n=4), academia (n=3), and veterinary pharmacy (n=1).

A total of eighty-six pharmacists answered the Post-Implementation Questionnaire – Malta (PostIQM). From these participants, thirty-six were male and fifty were female. The mean age of these participants was thirty-five years old and ranged from twenty-two to fifty-eight years of age. Forty-seven participants had 1–10 years of experience, twenty-two had 11–20, eleven had 21–30, and six had over 30 years of experience. Twenty-one participants were hospital pharmacists, twenty-eight participants were community pharmacists, twelve participants worked in wholesale dealing, eleven participants worked in regulatory science, five participants were industrial pharmacists, and nine participants listed another pharmaceutical sector – these included medical representation (n=7), and academia (n=2).

A total of seventeen pharmacists answered the Post-Implementation Questionnaire-Bonn (PostIQB). From these participants, five were male and twelve were female. The mean age of these participants was thirty-six years and ranged from twenty-four to sixty-five years of age. Twelve participants had 1–10 years of experience, one had 11–20, three had 21–30, and one had over 30 years of experience. All seventeen participants were community pharmacists.

3.3 Encounter with Falsified Medicines

Out of the eighty-five participants who answered the PreIQ, seven reported having encountered cases of falsified medication during their practice. Of those who reported having dealt with cases of falsified medication, two were community pharmacists, four worked in wholesale dealing, and one worked in industrial pharmacy.

Out of the eighty-six participants who answered the PostIQM, fourteen reported having encountered falsified medicines during their practice. Out of these eighty-six, two worked in wholesale dealing, three in regulatory sciences, four in community pharmacy, two were medical representatives, two in hospital pharmacy, one in industrial pharmacy, and two were medical representatives.

Out of the seventeen participants who answered the PostIQB, two reported having encountered falsified medicines during their practice.

Table 3.2 shows an increase of 8.1% in participants having encountered cases of medicine falsifications during their practice before and after the implementation of the UI in Malta, however this percentage increment is not significant since the p-value (0.109) exceeds the 0.05 level of significance.

Table 3.2: Comparison of Pre-Implementation Questionnaire (PreIQ) (N=85) and Post-Implementation Questionnaire-Malta (PostIQM) (N=86) Participants having Encountered Falsified Medicines During their Practice

			PreIQ	PostIQM	Total
Have you ever encountered a case of medicine falsification during your practice?	Yes	Count	7	14	21
		Percentage	8.2%	16.3%	12.3%
	No	Count	78	72	150
		Percentage	91.8%	83.7%	87.7%
Total		Count	85	86	171
		Percentage	100.0%	100.0%	100.0%

$X^2(1) = 2.568$, $p = 0.109$

Table 3.3 shows a 4.5% difference in participants having encountered cases of medicine falsifications in Malta and Bonn after the implementation of the UI, however this difference is not significant.

Table 3.3: Comparison of Post-Implementation Questionnaire – Malta (PostIQM) (N=86) and Post-Implementation Questionnaire – Bonn (PostIQB) (N=17) Participants having Encountered Falsified Medicines During their Practice

			PostIQM	PostIQB	Total
Have you ever encountered a case of medicine falsification during your practice?	Yes	Count	14	2	16
		Percentage	16.3%	11.8%	15.5%
	No	Count	72	15	87
		Percentage	83.7%	88.2%	84.5%
Total		Count	86	17	103
		Percentage	100.0%	100.0%	100.0%

$X^2(1) = 0.220$, $p = 0.639$

3.4 Knowledge Regarding the UI

This section presents how and when participants first heard of the UI, as well as their knowledge about the components and function of the UI.

3.4.1 Awareness of the UI

Out of the eighty-five participants who answered the PreIQ, twenty-three reported having heard of the introduction of the UI via official correspondence. The Chamber of Pharmacists and the Malta Medicines Authority were the most commonly listed sources of official correspondence. Other participants heard of the UI from work colleagues (n=42), mass media (n=15), social media (n=2), and other sources (n=12).

Out of the eighty-six participants who answered the PostIQM, thirty-six heard of the UI via official correspondence. The most commonly cited sources being the Chamber of Pharmacists and the Malta Medicines Authority. Forty-five participants heard of the UI from work colleagues, eight from mass media, nine from social media, and nine others reported having heard of the UI from other sources.

Out of the seventeen participants who answered the PostIQB, eight heard of the UI via official correspondence, including from regional pharmacy associations, e.g. Sonderrundschreiben von Apothekerverband, and national pharmacy associations, e.g. Pharmazeutische Zeitung. Five heard about the UI from their work colleagues, two from mass media, one from social media, and one participant listed other sources. Participants answering this question had the option of choosing more than one answer.

The majority of participants surveyed in the PreIQ stated that they had first heard about the introduction of the UI in 2018 (n=40). Other participants first heard of the UI before 2018 (n=33), or in January of 2019 (n=12).

In the PostIQM, most participants had first heard about the UI before 2018 (n=41). Thirty-three participants first heard of the UI in 2018, and 12 in 2019-2020.

The majority of participants who answered the PostIQB had first heard of the UI in 2019 (x=11). One participant had heard of the UI in the month prior to participating in the study, four participants heard of the UI before 2018, and one other participant listed first hearing of the UI at another time.

3.4.2 Components of the UI

In the PreIQ the majority of participants stated that they were aware of the components making up the UI (n=49). Participants were then asked to choose which elements made up the UI from a list containing the four correct options and one incorrect option. Out of those who answered the previous question in the affirmative, eleven gave a correct answer in the subsequent question.

In the PostIQM and PostIQB the majority of participants also stated that they were aware of the components making up the UI (PostIQM: n=66; PostIQB: n=13). Out of these, twenty-one gave a correct answer in the PostIQM and one answered correctly in the PostIQB when asked to choose the components that make up the UI.

Table 3.4 shows an increase of 19.1% in participants who reported knowing the components of the UI before and after the implementation of the UI in Malta. This percentage increment is significant since the p-value (0.008) does not exceed the 0.05 level of significance.

Table 3.4: Comparison of Pre-Implementation Questionnaire (PreIQ) (N=85) and Post-Implementation Questionnaire-Malta (PostIQM) (N=86) Participants Stating they were Aware of the Components of the UI

			PreIQ	PostIQM	Total
Are you aware of the components of the unique identifier?	Yes	Count	49	66	115
		Percentage	57.6%	76.7%	67.3%
	No	Count	36	20	56
		Percentage	42.4%	23.3%	32.7%
Total		Count	85	86	171
		Percentage	100.0%	100.0%	100.0%

$X^2(1) = 7.079$, $p = 0.008$

Table 3.5 shows a 9.4% increase in participants who chose the correct components making up the UI, however this difference is not significant.

Table 3.5: Comparison of Pre-Implementation Questionnaire (PreIQ) (N=85) and Post-Implementation Questionnaire-Malta (PostIQM) (N=86) Participants who Correctly Listed the Components of the UI

			PreIQ	PostIQM	Total
If Yes, which of the following are components of the unique identifier?	Correct	Count	11	21	32
		Percentage	22.4%	31.8%	27.4%
	Incorrect	Count	38	45	85
		Percentage	77.6%	68.2%	72.6%
Total		Count	49	66	115
		Percentage	100.0%	100.0%	100.0%

$X^2(1) = 1.229$, $p = 0.268$

Table 3.6 shows a percentage difference of 0.2% in participants who reported knowing the components making up the UI in Malta and Bonn after the implementation of the UI. This percentage increment is not significant.

Table 3.6: Comparison of Post-Implementation Questionnaire – Malta (PostIQM) (N=86) and Post-Implementation Questionnaire – Bonn (PostIQB) (N=17) Participants Stating they were Aware of the Components of the UI

			PostIQM	PostIQB	Total
Are you aware of the components of the unique identifier?	Yes	Count	66	13	79
		Percentage	76.7%	76.5%	76.7%
	No	Count	20	4	24
		Percentage	23.3%	23.5%	23.3%
Total		Count	86	17	103
		Percentage	100.0%	100.0%	100.0%

$X^2(1) = 0.001$, $p = 0.981$

Table 3.7 shows a 24.1% difference in PostIQM and PostIQB participants who chose the correct components making up the UI, however this difference is not significant.

Table 3.7: Comparison of Post-Implementation Questionnaire – Malta (PostIQM) (N=86) and Post-Implementation Questionnaire – Bonn (PostIQB) (N=17) Participants who Correctly Listed the Components of the UI

			PostIQM	PostIQB	Total
If Yes, which of the following are components of the unique identifier?	Correct	Count	21	1	22
		Percentage	31.8%	7.7%	27.8%
	Incorrect	Count	45	12	57
		Percentage	68.2%	92.3%	72.2%
Total		Count	66	13	79
		Percentage	100.0%	100.0%	100.0%

$X^2(1) = 3.146$, $p = 0.076$

3.4.3 Function of the UI

In the PreIQ the majority of participants said that they knew the function of the UI (n=66). Participants were then asked to describe the function of the UI. Out of those who had reported knowing the function of the UI, forty-nine answered correctly and four left the question blank. Answers including the key phrases 'prevention of falsified medicines', or 'authentication of medicines' or similar phrases were deemed correct.

Seventy-seven participants PostIQM participants and sixteen PostIQB participants also stated that they knew the function of the UI. The majority also correctly described the function of the UI in the PostIQM (n=64) and the PostIQB (n=13). Five participants in the PostIQM left the question blank. The same criteria as in the PreIQ were used to determine whether an answer was correct.

Table 3.8 shows an increase of 11.9% in participants who reported knowing the function of the UI before and after the implementation of the UI in Malta. This percentage increment is significant.

Table 3.8: Comparison of Pre-Implementation Questionnaire (PreIQ) (N=85) and Post-Implementation Questionnaire-Malta (PostIQM) (N=86) Participants Stating they were Aware of the Function of the UI

			PreIQ	PostIQM	Total
Are you aware of the function of the unique identifier?	Yes	Count	66	77	143
		Percentage	77.6%	89.5%	83.6%
	No	Count	19	9	28
		Percentage	22.4%	10.5%	16.4%
Total		Count	85	86	171
		Percentage	100.0%	100.0%	100.0%

$X^2(1) = 4.412$, $p = 0.036$

Table 3.9 shows a 9.9% increase in participants who defined the UI correctly, however this difference is not significant.

Table 3.9: Comparison of Pre-Implementation Questionnaire (PreIQ) (N=85) and Post-Implementation Questionnaire-Malta (PostIQM) (N=86) Participants who Correctly Stated the Function of the UI

			PreIQ	PostIQM	Total
If Yes can you describe the function of the unique identifier?	Correct	Count	49	64	113
		Percentage	79.0%	88.9%	84.3%
	Incorrect	Count	13	8	21
		Percentage	21.0%	11.1%	15.7%
Total		Count	62	72	134
		Percentage	100.0%	100.0%	100.0%

$X^2(1) = 2.449$, $p = 0.118$

Table 3.10 shows a percentage difference of 4.6% in participants who reported knowing the function of the UI in Malta and Bonn after the implementation of the UI. This percentage increment is not significant.

Table 3.10: Comparison of Post-Implementation Questionnaire – Malta (PostIQM) (N=86) and Post-Implementation Questionnaire – Bonn (PostIQB) (N=17) Participants Stating they were Aware of the Function of the UI

			PostIQM	PostIQB	Total
Are you aware of the function of the unique identifier?	Yes	Count	77	16	93
		Percentage	89.5%	94.1%	90.3%
	No	Count	9	1	10
		Percentage	10.5%	5.9%	9.7%
Total		Count	86	17	103
		Percentage	100.0%	100.0%	100.0%

$X^2(1) = 0.340$, $p = 0.560$

Table 3.11 shows a 7.6% difference in PostIQM and PostIQB participants who gave a correct definition for the UI, however this difference is not significant.

Table 3.11: Comparison of Post-Implementation Questionnaire – Malta (PostIQM) (N=86) and Post-Implementation Questionnaire – Bonn (PostIQB) (N=17) Participants who Correctly Stated the Function of the UI

			PostIQM	PostIQB	Total
If Yes can you describe the function of the unique identifier?	Correct	Count	64	13	77
		Percentage	88.9%	81.3%	87.5%
	Incorrect	Count	8	3	11
		Percentage	11.1%	18.8%	12.5%
Total		Count	72	16	88
		Percentage	100.0%	100.0%	100.0%

$X^2(1) = 0.698$, $p = 0.403$

3.5 Decommissioning of National Health Service (NHS) Medication

In the PreIQ, a majority of participants stated that NHS medicinal packs dispensed in hospitals or community pharmacies (as part of the Pharmacy of Your Choice scheme) should have their UIs decommissioned just before dispensing to the patient by the pharmacist (n=43). Twenty-eight participants stated that NHS medicinal packs should be decommissioned before transportation to the hospital or community pharmacy, and twelve stated that this should take place upon arrival at the community pharmacy. Two participants stated that the decommissioning of NHS medication should take place at other points in the supply chain.

In the PostIQM most participants also stated that NHS medicinal packs dispensed in hospitals or community pharmacies should be decommissioned just before dispensing to the patient (n=63). Eleven participants stated that NHS medicinal packs should be

decommissioned before transportation to the hospital or community pharmacy, and six stated that this should take place upon arrival at the community pharmacy. Six participants were of the opinion that NHS medicinal packs should be decommissioned at other times.

In the PostIQB, eight participants stated that NHS medicinal packs dispensed in hospitals or community pharmacies should be decommissioned just before dispensing to the patient, three participants stated that NHS medicinal packs should be decommissioned before transportation to the hospital or community pharmacy, and five stated that this should take place upon arrival at the community pharmacy. One participant stated that NHS medication should be decommissioned at other times.

Table 3.12 shows a decrease of 20.1% in participants who preferred that NHS medication packs be decommissioned before being transported to the hospital or community pharmacy, a 7.1% decrease in participants who preferred that decommissioning of these packs takes place upon arrival at the hospital or community pharmacy, and a 22.7% increase in participants who preferred that decommissioning be carried out just before a pack is dispensed to the patient, before and after the implementation of the UI in Malta. These percentage increments are significant.

Table 3.12: Comparison of Pre-Implementation Questionnaire (PreIQ) (N=85) and Post-Implementation Questionnaire-Malta (PostIQM) (N=86) Participants' Opinions on the Point of Decommissioning for NHS Medications

			PreIQ	PostIQM	Total
At which point should decommissioning of the unique identifier take place for National Health Service medication in a hospital or community pharmacy?	Before Being Transported to the Community Pharmacy	Count	28	11	39
		Percentage	32.9%	12.8%	22.8%
	Upon Arrival at the Community Pharmacy	Count	12	6	18
		Percentage	14.1%	7.0%	10.5%
	Just Before Being Dispensed by Community Pharmacist	Count	43	63	106
		Percentage	50.6%	73.3%	62.0%
	Other	Count	2	6	8
		Percentage	2.4%	7.0%	4.7%
Total		Count	85	86	171
		Percentage	100.0%	100.0%	100.0%

$X^2(3) = 15.179$, $p = 0.002$

Table 3.13 shows a difference of 4.8% in participants who preferred that NHS medication packs be decommissioned before being transported to the hospital or community pharmacy, a 22.4% difference in participants who preferred that decommissioning of these packs takes place upon arrival at the hospital or community pharmacy, and a 26.2% difference in participants who preferred that decommissioning be carried out just before a pack is dispensed to the patient, before and after the implementation of the UI in Malta. These percentage increments are significant.

Table 3.13: Comparison of Post-Implementation Questionnaire – Malta (PostIQM) (N=86) and Post-Implementation Questionnaire – Bonn (PostIQB) (N=17) Participants' Opinions on the Point of Decommissioning for NHS Medications

			PostIQM	PostIQB	Total
At which point should decommissioning of the unique identifier take place for National Health Service medication in a hospital or community pharmacy?	Before Being Transported to the Community Pharmacy	Count	11	3	14
		Percentage	12.8%	17.6%	13.6%
	Upon Arrival at the Community Pharmacy	Count	6	5	11
		Percentage	7.0%	29.4%	10.7%
	Just Before Being Dispensed by Community Pharmacist	Count	63	8	71
		Percentage	73.3%	47.1%	68.9%
	Other	Count	6	1	7
		Percentage	7.0%	5.9%	6.8%
Total		Count	86	17	103
		Percentage	100.0%	100.0%	100.0 %

$X^2(3) = 8.374$, $p = 0.039$

3.6 OTC Products and the UI

The majority of participants in both the PreIQ (n=55) and PostIQM (n=56) did not agree with the exclusion of OTC products from bearing the UI. The most commonly cited reason for this being that OTC products are also at risk of falsification, therefore decreasing patient safety. Most participants who agreed with the exemption for OTC products from bearing the UI stated that OTC products are less likely to be targeted for falsification compared to POMs due to their relative cheapness, therefore making tracing and authentication of OTC packs less necessary than for POMs.

In the PostIQB the majority of participants agreed with the exclusion of OTC production from bearing the UI (n=13). As in the PreIQ and PostIQM the most commonly given reasons for this was the decreased risk of OTC product being targeted for falsification.

Table 3.14 shows a decrease of 0.4% in participants who agreed that OTC products should be exempted from bearing the UI, before and after the implementation of the UI in Malta, however this percentage increment is not significant.

Table 3.14: Comparison of Pre-Implementation Questionnaire (PreIQ) (N=85) and Post-Implementation Questionnaire-Malta (PostIQM) (N=86) Participants' Opinions on the Exemption of OTC Products from Bearing the UI

			PreIQ	PostIQM	Total
Do you agree with the decision by the EU to exclude OTC products from bearing the unique identifier?	Yes	Count	30	30	60
		Percentage	35.3%	34.9%	35.1%
	No	Count	55	56	111
		Percentage	64.7%	65.1%	64.9%
Total		Count	85	86	171
		Percentage	100.0%	100.0%	100.0%

$X^2(1) = 0.003$, $p = 0.955$

Table 3.15 shows a 41.6% difference in participants who agreed that OTC products should be exempted from bearing the UI, in Malta and Bonn after the implementation of the UI. This difference is significant.

Table 3.15: Comparison of Post-Implementation Questionnaire – Malta (PostIQM) (N=86) and Post-Implementation Questionnaire – Bonn (PostIQB) (N=17) Participants' Opinions on the Exemption of OTC Products from Bearing the UI

			PostIQM	PostIQB	Total
Do you agree with the decision by the EU to exclude OTC products from bearing the unique identifier?	Yes	Count	30	13	43
		Percentage	34.9%	76.5%	41.7%
	No	Count	56	4	60
		Percentage	65.1%	23.5%	58.3%
Total		Count	86	17	103
		Percentage	100.0%	100.0%	100.0%

$X^2(1) = 10.094$, $p = 0.001$

3.7 Exemptions from Introducing the UI

In the PreIQ and PostIQM participants were asked whether Malta should have been exempted from the introduction of the UI. The majority of participants in the PreIQ (n=78) and in the PostIQM (n=77) disagreed with this statement. The most common reasons given for this was that, due to being part of the EU, Malta should follow the same rules as the rest of the union, and that being exempted from the introduction of the UI would put Maltese patients at increased risk of adverse effects from falsified medication. In both the PreIQ and PostIQM, the most commonly cited reasons by those who agreed that Malta should have been exempted from bearing the UI was the increase in workload and the decreased risk of falsified medicines entering the Maltese market due to its small size.

Table 3.16 shows an increase of 2.3% in participants who agreed that Malta should be exempted from introducing the UI, before and after the implementation of the UI in Malta, however this percentage increment is not significant.

Table 3.16: Comparison of Pre-Implementation Questionnaire (PreIQ) (N=85) and Post-Implementation Questionnaire-Malta (PostIQM) (N=86) Participants' Opinions on the Exemption of Malta from Introducing the UI

			PreIQ	PostIQM	Total
Should Malta have been exempted from introducing the unique identifier?	Yes	Count	7	9	16
		Percentage	8.2%	10.5%	9.4%
	No	Count	78	77	155
		Percentage	91.8%	89.5%	90.6%
Total		Count	85	86	171
		Percentage	100.0%	100.0%	100.0%

$X^2(1) = 0.251$, $p = 0.617$

In the PostIQB participants were asked if there should have been any exemptions from introducing the UI. The majority disagreed that there should be any such exemptions (n=13). Reasons given for this included that this would put patients at risk and introduce holes in the system that would allow falsified medicines to penetrate the legal supply chain. Reasons given by those participants who agreed that there should be exemptions to the introduction of the UI included that exemptions should be made for drugs that cost from 1-100euros and for drugs that are urgently needed.

3.8 UI Impact on Man-Hours Required

The majority of participants in the PreIQ (n=73), PostIQM (n=75), and PostIQB (n=12), agreed that the UI causes an increase in the number of man-hours required in their workplace. Participants who had agreed with the previous statement were then asked

to choose how many additional man-hours would be required per week as a result of the introduction of the UI. The answers given in the PreIQ, PostIQM, and PostIQB are shown in figures 3.1, 3.2, and 3.3 respectively, with the majority of participants in all three questionnaires stating that the increase was of five hours/week or of ten hours/week.

Figure 3.1: Number of Participants in the PreIQ (N=85) who Agreed that the UI will Increase the Number of Man-Hours Required per week

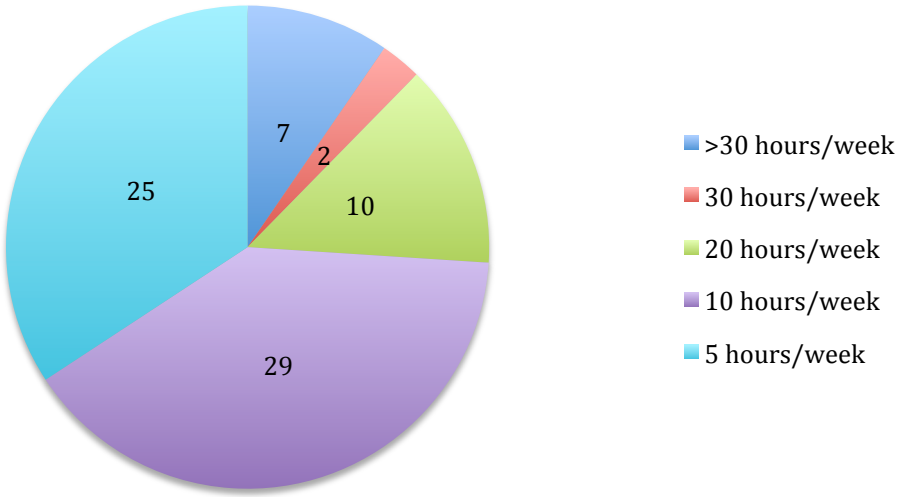

Figure 3.2: Number of participants in the PostIQB (N=17) who agreed that the UI increased the number of man-hours required per week

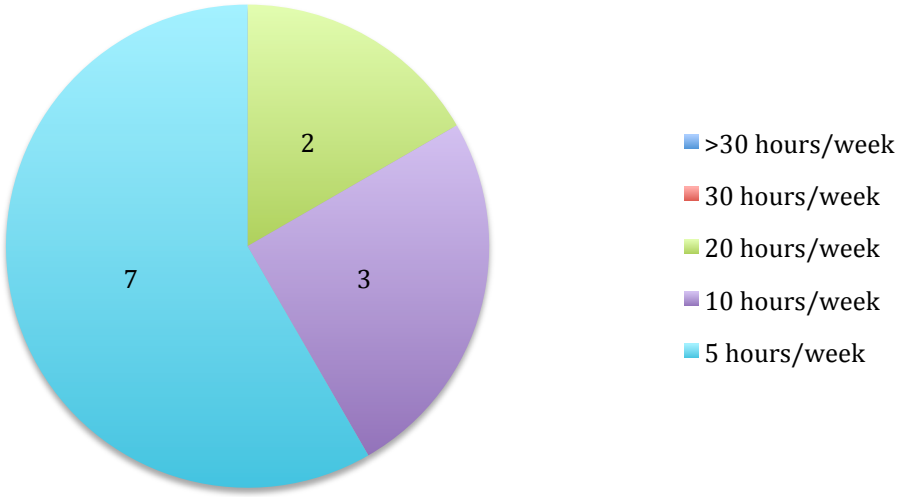

Figure 3.3: Number of Participants in the PostIQM (N=86) who agreed that the UI Increased the Number of Man-Hours Required Per Week

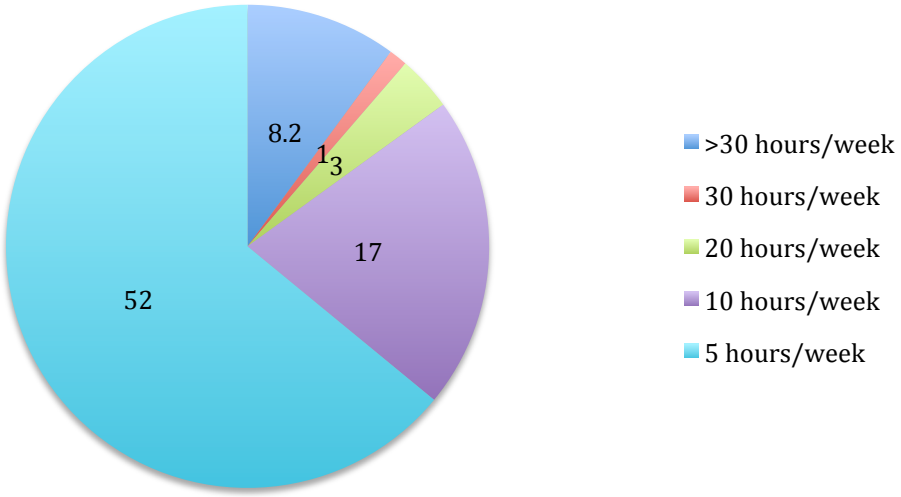

Table 3.17 shows an 1.3% increase in participants who agreed that the UI increases the number of man-hours required per week, before and after the implementation of the UI in Malta, however this percentage increment is not significant.

Table 3.17: Comparison of Pre-Implementation Questionnaire (PreIQ) (N=85) and Post-Implementation Questionnaire-Malta (PostIQM) (N=86) Participants' Opinions on whether the UI Increased the Number of Man-Hours Required

			PreIQ	PostIQM	Total
Does the introduction of the unique identifier cause an increase in the amount of man hours required?	Yes	Count	73	75	148
		Percentage	85.9%	87.2%	86.5%
	No	Count	12	11	23
		Percentage	14.1%	12.8%	13.5%
Total		Count	85	86	171
		Percentage	100.0%	100.0%	100.0%

$X^2(1) = 0.065$, $p = 0.799$

Table 3.18 shows an increase of 35.1% in participants who stated that the UI increases the number of man-hours required by 5 hours/week, and percentage decreases of 17%, 9.7%, 1.4%, and 6.9% in participants who stated that the increase is of 10 hours/week, 20 hours/week, 30 hours/week, and >30 hours/week, respectively. These percentage increments are significant.

Table 3.18: Comparison of Pre-Implementation Questionnaire (PreIQ) (N=85) and Post-Implementation Questionnaire-Malta (PostIQM) (N=86) Participants' Opinions on How Many More Man-Hours would be Required Per Week due to the UI

			PreIQ	PostIQM	Total
If Yes, how many additional man hours are required per week?	5 Hrs/Week	Count	25	52	77
		Percentage	34.2%	69.3%	52.0%
	10 Hrs/Week	Count	29	17	46
		Percentage	39.7%	22.7%	31.1%
	20 Hrs/Week	Count	10	3	13
		Percentage	13.7%	4.0%	8.8%
	30 Hrs/Week	Count	2	1	3
		Percentage	2.7%	1.3%	2.0%
	>30 Hrs/Week	Count	7	2	9
		Percentage	9.6%	2.7%	6.1%
Total		Count	73	75	148
		Percentage	100.0%	100.0%	100.0%

$X^2(4) = 19.455$, $p = 0.001$

Table 3.19 shows a difference of 16.6% in participants who agreed that the UI increases the number of man-hours required, after the implementation of the UI in Malta and Bonn, however this percentage increment is not significant.

Table 3.19: Comparison of Post-Implementation Questionnaire – Malta (PostIQM) (N=86) and Post-Implementation Questionnaire - Bonn (PostIQB) (N=17) Participants' Opinions on whether the UI Increased the Number of Man-Hours Required

			PostIQM	PostIQB	Total
Does the introduction of the unique identifier cause an increase in the amount of man hours required?	Yes	Count	75	12	87
		Percentage	87.2%	70.6%	84.5%
	No	Count	11	5	16
		Percentage	12.8%	29.4%	15.5%
Total		Count	86	17	103
		Percentage	100.0%	100.0%	100.0%

$X^2(1) = 2.989$, $p = 0.084$

Table 3.20 shows differences of 11%, 2.3%, 12.7%, 1.3%, and 2.7% in participants who stated that the UI increases the number of man-hours required by 5 hours/week, 10 hours/week, 20 hours/week, 30 hours/week, and >30 hours/week, respectively. These percentage increments are not significant.

Table 3.20: Comparison of Post-Implementation Questionnaire – Malta (PostIQM) (N=86) and Post-Implementation Questionnaire - Bonn (PostIQB) (N=17) Participants' Opinions on How Many More Man-Hours would be Required Per Week due to the UI

			PostIQM	PostIQB	Total
If Yes, how many additional man-hours are required per week?	5 Hrs/Week	Count	52	7	59
		Percentage	69.3%	58.3%	67.8%
	10 Hrs/Week	Count	17	3	20
		Percentage	22.7%	25.0%	23.0%
	20 Hrs/Week	Count	3	2	5
		Percentage	4.0%	16.7%	5.7%
	30 Hrs/Week	Count	1	0	1
		Percentage	1.3%	0.0%	1.1%
	>30 Hrs/Week	Count	2	0	2
		Percentage	2.7%	0.0%	2.3%
Total		Count	75	12	87
		Percentage	100.0%	100.0%	100.0%

$X^2(4) = 3.577$, $p = 0.466$

3.9 Falsified Medicines in the EU

The majority of participants who answered the PreIQ, PostIQM, and PostIQB, strongly agreed or agreed that entry of falsified medicines into the legal supply chain was a problem in the EU (PreIQ: n=57; PostIQM: n=49; PostIQB: n=9), that the UI decreases the number of falsified medicines entering the EU via the legal supply chain (PreIQ: n=69; PostIQM: n=48; PostIQB: n=11), and that the UI is a proportional response to the problem of falsified medicines in EU countries (PreIQ: n=46; PostIQM: n=53; PostIQB: n=12). These results are shown in figure 3.4.

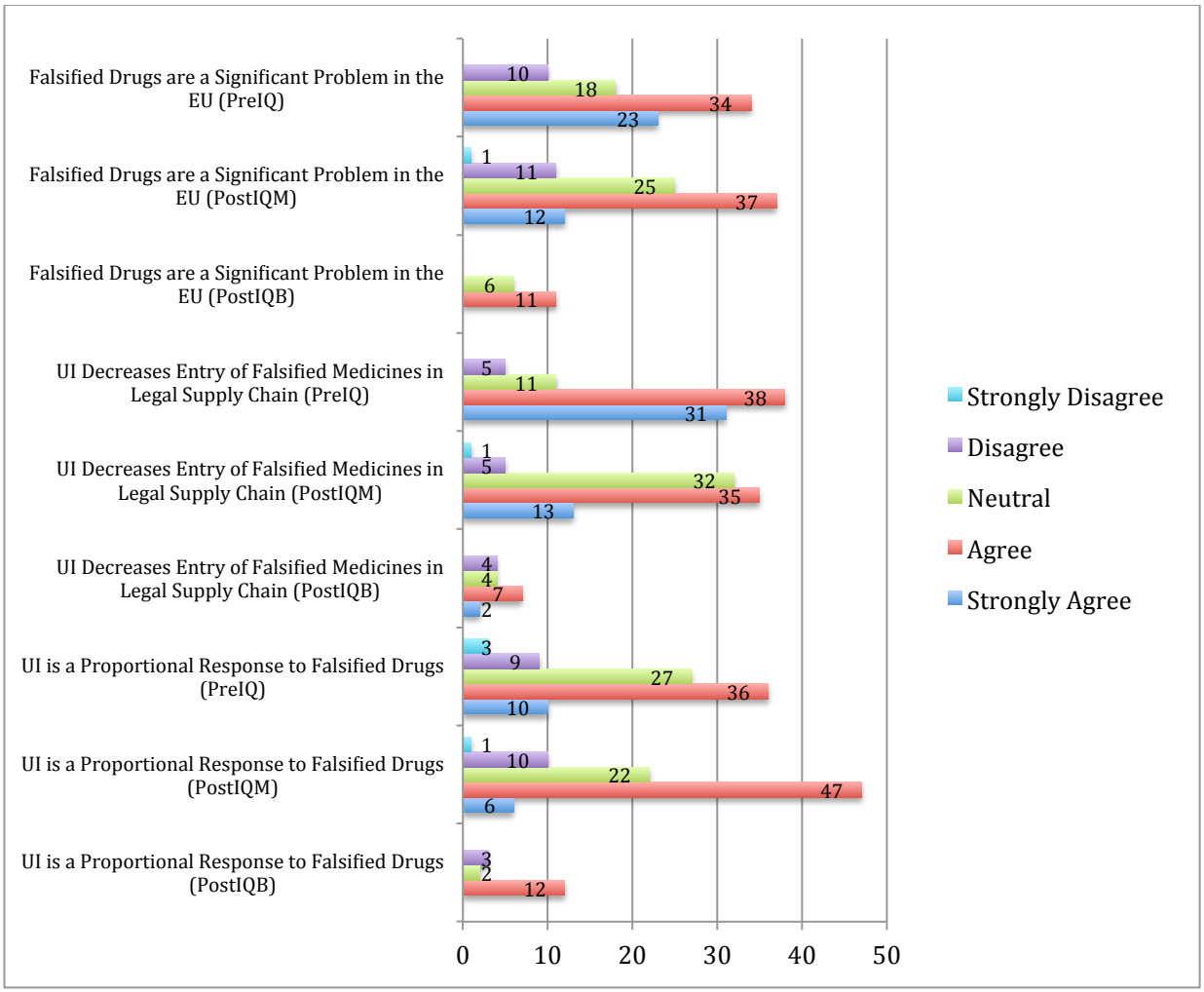

Figure 3.4: Number of Pharmacists in the PreIQ (N=85), PostIQM (N=86), and PostIQB (N=17) who Answered Strongly Agree, Agree, Neutral, Disagree, or Strongly Disagree to the Above Statements Regarding Falsified Medicines in the EU

Table 3.21 shows that a non-significant decrease was present in the mean rating score of responses in the PreIQ and PostIQM to the statement that entry of falsified medicines into the legal supply chain is a problem in EU countries. This means that less participants agreed with this statement in the PostIQM compared to the PreIQ. A non-significant increase was present in the mean rating score of responses to the statement that the UI is a proportional response to falsified medicines in EU countries, meaning that more participants agreed with this statement in the PostIQM compared to the PreIQ (Table 3.21). A significant decrease was present in the mean rating score of responses to the statement that the UI decreases the entry of falsified medicines in the legal supply chain, meaning that agreement with this statement in the PostIQM was significantly less than in the PreIQ (Table 3.21).

Table 3.21: Comparison of Pre-Implementation Questionnaire (PreIQ) (N=85) and Post-Implementation Questionnaire-Malta (PostIQM) (N=86) Mean Rating Scores Regarding Falsified Medicines in the EU

		Sample size	Mean	Std. Dev.	P-value
Entry of falsified medicines into the legal supply chain is a significant problem in EU countries.	PreIQ	85	3.82	.966	0.060
	PostIQM	86	3.56	.928	
The introduction of the UI results in a significant decrease in the entry of falsified medicines within the Legal Supply Chain	PreIQ	85	4.12	.851	0.000
	PostIQM	86	3.63	.855	
The introduction of the UI is a proportional response to the problem of falsified medicines in EU countries	PreIQ	85	3.48	.959	0.637
	PostIQM	86	3.55	.835	

Table 3.22 shows that non-significant differences were present between the mean rating scores of statements in the PostIQM and PostIQB regarding the entry of falsified medicines into the legal supply chain in the EU. It also shows that the UI results in a decrease in the entry of falsified medicines into the legal supply chain, and that the UI is a proportional response to falsified medicines in the EU. Fewer participants agreed with the latter two statements in the PostIQB compared to the PostIQM, while more participants agreed with the first statement in the PostIQB compared to the PostIQM.

Table 3.22: Comparison of Post-Implementation Questionnaire – Malta (PostIQM) (N=86) and Post-Implementation Questionnaire - Bonn (PostIQB) (N=17) Mean Rating Scores Regarding Falsified Medicines in the EU

		Sample size	Mean	Std. Dev.	P-value
Entry of falsified medicines into the legal supply chain is a significant problem in EU countries	PostIQM	86	3.56	.928	0.801
	PostIQB	17	3.65	.493	
The introduction of the unique identifier results in a significant decrease in the entry of falsified medicines within the Legal Supply Chain	PostIQM	86	3.63	.855	0.442
	PostIQB	17	3.41	1.004	
The introduction of the unique identifier is a proportional response to the problem of falsified medicines in EU countries.	PostIQM	86	3.55	.835	0.929
	PostIQB	17	3.53	.800	

3.10 Preparedness and Information Regarding the UI

The majority of participants who answered the PreIQ, PostIQM, and PostIQB remained neutral, disagreed, or strongly disagreed, when answering whether they had enough time to prepare for the introduction of the UI (PreIQ: n=69; PostIQM: n=50; PostIQB: n=9), and whether there is enough information available for patients regarding the UI (PreIQ: n=80; PostIQM: n=77; PostIQB: n=15). The majority who answered the PreIQ

and PostIQM also remained neutral, disagreed, or strongly disagreed that enough information was available for pharmacists regarding the UI (PreIQ: n=57; PostIQM: n=53), while a majority of participants who answered the PostIQB strongly agreed or agreed with this statement (n=10). These results are shown in figure 3.5.

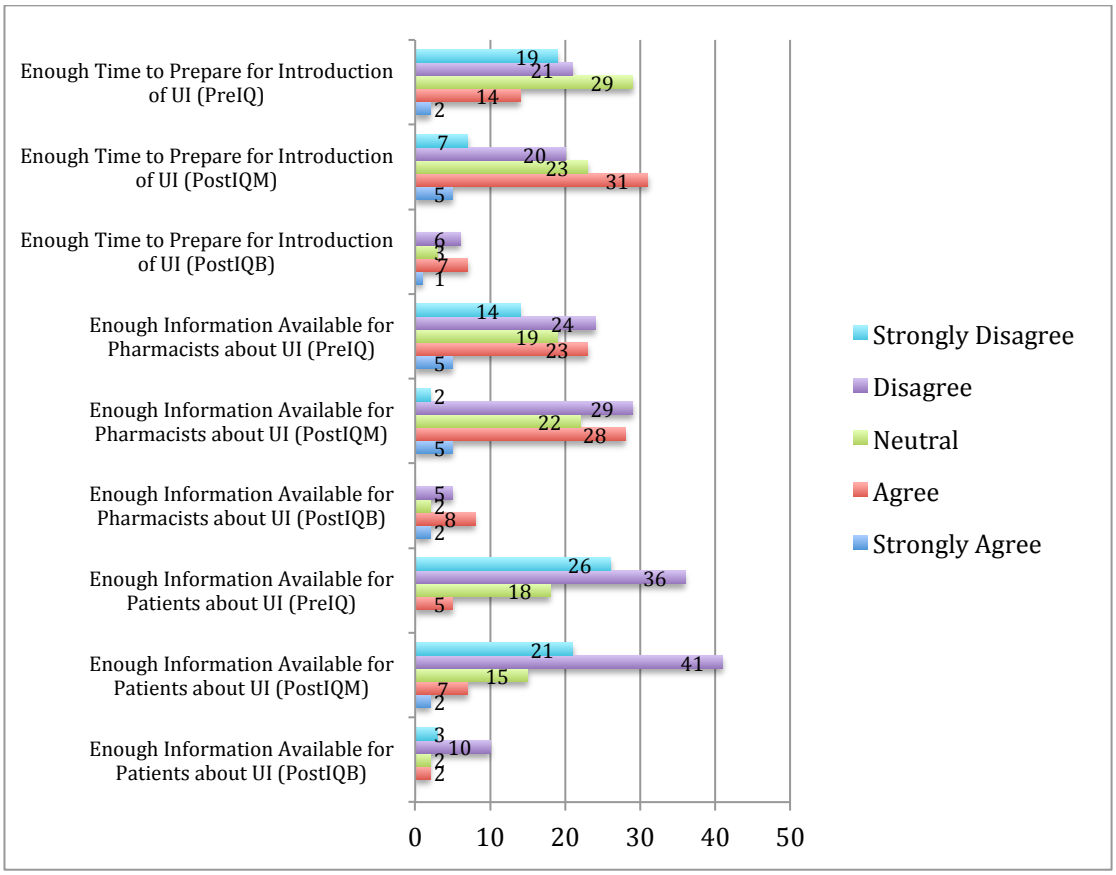

Figure 3.5: Number of Pharmacists in the PreIQ (N=85), PostIQM (N=86), and PostIQB (N=17) who Answered Strongly Agree, Agree, Neutral, Disagree, or Strongly Disagree to the Above Statements Regarding Preparedness and Information on the UI

Table 3.23 shows a significant increase in the mean rating scores of participants' responses in the PreIQ and PostIQM to the statement that they had enough time to prepare for the introduction of the UI, while non-significant increases were present in the mean rating scores of participants' responses in the PreIQ and PostIQM for the statements that enough information is available for pharmacists and patients regarding the UI.

Table 3.23: Comparison of Pre-Implementation Questionnaire (PreIQ) (N=85) and Post-Implementation Questionnaire-Malta (PostIQM) (N=86) Participants' Opinions Regarding Preparedness and Information on the UI

		Sample size	Mean	Std. Dev.	P-value
You had enough time to prepare for the introduction of the unique identifier.	PreIQ	85	2.52	1.087	0.001
	PostIQM	86	3.08	1.076	
There is enough information available for pharmacists about the unique identifier.	PreIQ	85	2.78	1.189	0.117
	PostIQM	86	3.06	.998	
There is enough information available for patients about the unique identifier	PreIQ	85	2.02	.873	0.440
	PostIQM	86	2.16	.968	

Table 3.24 shows non-significant differences in the mean rating scores of participants' responses in the PostIQM and PostIQB to the statements that they had enough time to prepare for the introduction of the UI, and that there is enough information available for patients and pharmacists on the UI. In all three cases, PostIQB participants agreed more with these statements compared to PostIQM participants.

Table 3.24: Comparison of Post-Implementation Questionnaire – Malta (PostIQM) (N=86) and Post-Implementation Questionnaire – Bonn (PostIQB) (N=17) Participants' Opinions Regarding Preparedness and Information on the UI

		Sample size	Mean	Std. Dev.	P-value
You had enough time to prepare for the introduction of the unique identifier	PostIQM	86	3.08	1.076	0.791
	PostIQB	17	3.18	1.015	
There is enough information available for pharmacists about the unique identifier	PostIQM	86	3.06	.998	0.197
	PostIQB	17	3.41	1.064	
There is enough information available for patients about the unique identifier	PostIQM	86	2.16	.968	0.882
	PostIQB	17	2.18	.883	

3.11 Financial Impact of the UI

The majority of participants who answered the PreIQ, PostIQM, and PostIQB remained neutral, disagreed, or strongly disagreed: that any potential benefits of the UI are worth the financial impact on their sector (PreIQ: n=51; PostIQM: n=57; PostIQB: n=14), that the introduction of the UI will attract more investment by pharmaceutical companies (PreIQ: n=74; PostIQM: n=71; PostIQB: n=12), that the introduction of the UI will allow pharmaceutical companies to increase their profits in the long run (PreIQ: n=50; PostIQM: n=59; PostIQB: n=17), that the immediate financial impact as a result of the introduction of the UI is risky for the Maltese/German/EU markets (PreIQ: n=62; PostIQM: n=64; PostIQB: n=14), and that the introduction of the UI causes money to be saved as a result of less hospitalisations from intake of falsified medicines (PreIQ: n=59; PostIQM: n=76; PostIQB: n=15). These results are shown in figure 3.6.

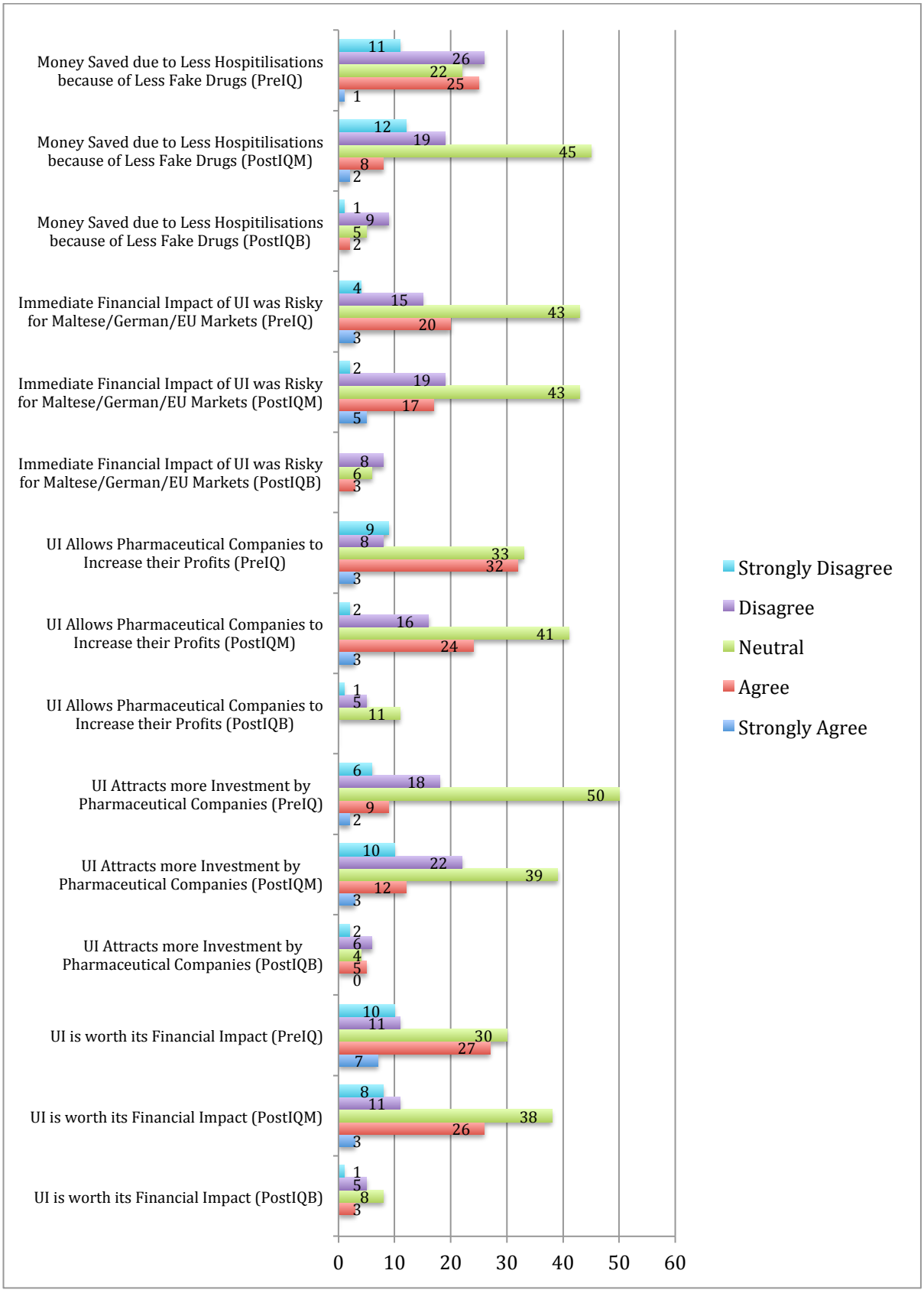

Figure 3.6: Number of Pharmacists in the PreIQ (N=85), PostIQM (N=86), and PostIQB (N=17) who Answered Strongly Agree, Agree, Neutral, Disagree, or Strongly Disagree to the Above Statements Regarding the Financial Impact of the UI

Table 3.25 shows that non-significant decreases are present in the mean rating scores provided to the statements in the PreIQ and PostIQM that benefits of the UI are worth its financial impact, that the UI will attract more pharmaceutical companies to invest in Malta, that the UI will cause pharmaceutical companies to increase their profits, and that the UI will cause money to be saved due to less hospitalizations as a result of intake of fake drugs. Fewer PostIQM participants agreed with these statements compared to PreIQ participants. A non-significant increase was also present in the mean rating score provided to the statement that the immediate financial impact of the UI might be risky for the Maltese market, meaning that more PostIQM participants agreed with this statement compared to PreIQ participants.

Table 3.25: Comparison of Pre-Implementation Questionnaire (PreIQ) (N=85) and Post-Implementation Questionnaire-Malta (PostIQM) (N=86) Participants' Opinions Regarding Financial Impact of the UI

		Sample size	Mean	Std. Dev.	P-value
Any potential benefits of the UI are worth the financial impact it has on your sector.	PreIQ	85	3.12	1.117	0.614
	PostIQM	86	3.06	.974	
The introduction of the UI attracts more pharmaceutical companies to invest in Malta.	PreIQ	85	2.80	.814	0.523
	PostIQM	86	2.72	.966	
The introduction of the UI allows pharmaceutical companies to increase their profits in the long run	PreIQ	85	3.14	1.014	0.449
	PostIQM	86	3.12	.832	
The immediate financial impact posed by the introduction of the UI is risky for the Maltese Market.	PreIQ	85	3.04	.865	0.869
	PostIQM	86	3.05	.866	
The introduction of the UI causes a significant amount of money to be saved due to less hospitalisations as a direct result of intake of fake drugs.	PreIQ	85	2.75	1.057	0.453
	PostIQM	86	2.64	.919	

Table 3.26 shows that a significant difference was present between the mean rating scores provided to the statement in the PostIQM and PostIQB that the UI will allow pharmaceutical companies to increase their profits, with more PostIQM participants agreeing with this statement compared to PostIQB participants. Non-significant differences in the mean rating scores provided to the other statements listed in table 3.25, with fewer PostIQB participants agreeing with these statements compared to PostIQM participants.

Table 3.26: Comparison of Post-Implementation Questionnaire – Malta (PostIQM) (N=86) and Post-Implementation Questionnaire - Bonn (PostIQB) (N=17) Participants' Opinions Regarding Financial Impact of the UI

		Sample size	Mean	Std. Dev.	P-value
Any potential benefits of the unique identifier are worth the financial impact it has on your sector	PostIQM	86	3.06	.974	0.169
	PostIQB	17	2.76	.831	
The introduction of the unique identifier attracts more investment by pharmaceutical companies	PostIQM	86	2.72	.966	0.970
	PostIQB	17	2.71	1.047	
The introduction of the Unique identifier allows pharmaceutical companies to increase their profits in the long run	PostIQM	86	3.12	.832	0.013
	PostIQB	17	2.59	.618	
The immediate financial impact posed by the introduction of the unique identifier is risky for the Maltese/German/EU market	PostIQM	86	3.05	.866	0.112
	PostIQB	17	2.71	.772	
The introduction of the unique identifier causes a significant amount of money to be saved due to less hospitalisations as a direct result of intake of fake drugs.	PostIQM	86	2.64	.919	0.320
	PostIQB	17	2.47	.800	

3.12 Impact of the UI on Medicine Accessibility

The majority of participants who answered the PreIQ, PostIQM, and the PostIQB remained neutral, disagreed, or strongly disagreed that the introduction of the UI negatively impacts accessibility to medicines (PreIQ: n=63; PostIQM: n=66; PostIQB:

n=12). A majority of participants who answered the PreIQ strongly agreed or agreed that the introduction of the UI will cause drug prices to increase (n=46), while a majority in the PostIQM and PostIQB remained neutral, disagreed, or strongly disagreed with this statement (PostIQM: n=63; PostIQB: n=17). A majority of those who answered the PreIQ also strongly agreed or agreed that Malta's dependence on 126(a) products, parallel trade products and small and medium enterprises means that it is hit harder with respect to accessibility to medicines than other EU countries (n=48), while a majority of those who answered the PostIQM disagreed with this statement (n=52). These results are shown in figure 3.7.

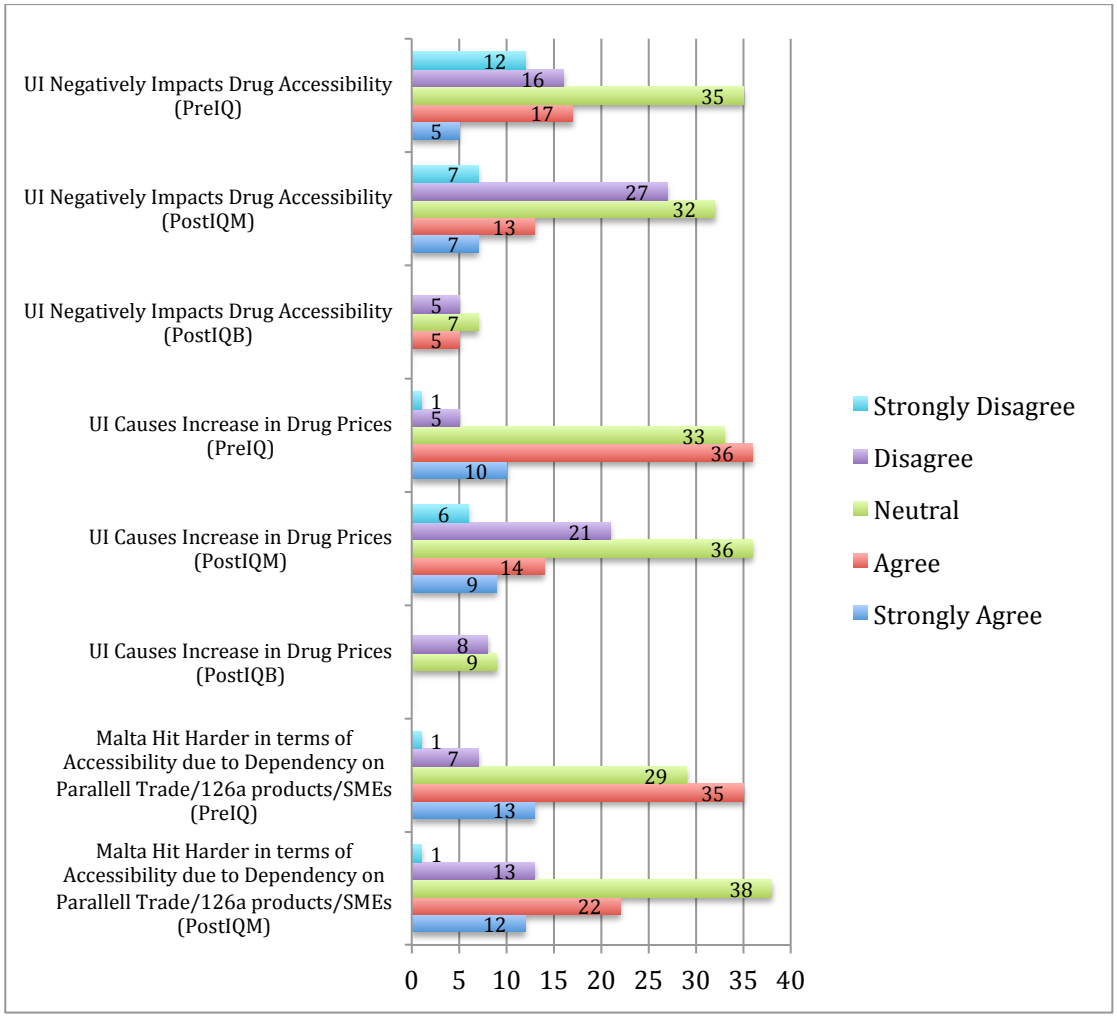

Figure 3.7: Number of Pharmacists in the PreIQ (N=85), PostIQM (N=86), and PostIQB (N=17) who Answered Strongly Agree, Agree, Neutral, Disagree, or Strongly Disagree to the Above Statements Regarding Impact of the UI on Medicine Accessibility

Table 3.27 shows that significant decreases were present for the mean rating scores provided to the statements in the PreIQ and PostIQM regarding Malta's dependence on 126(a) products, parallel trade products and SMEs, and increase in drug prices due to the UI, with fewer PostIQM participants agreeing with these statements compared to PreIQ participants. A non-significant decrease was also present for the mean rating score provided to the statement that the UI impacted medicine accessibility in Malta, with fewer PostIQM participants agreeing with this compared to PreIQ participants.

Table 3.27: Comparison of Pre-Implementation Questionnaire (PreIQ) (N=85) and Post-Implementation Questionnaire-Malta (PostIQM) (N=86) Participants' Opinions Regarding UI Impact on Medicine Accessibility

		Sample size	Mean	Std. Dev.	P-value
The introduction of the unique identifier negatively impacts the accessibility of medicines in Malta	PreIQ	85	2.85	1.086	0.723
	PostIQM	86	2.84	1.050	
Malta's dependence on 126(a) products, parallel trade products and small and medium enterprises means that it is hit harder with respect to accessibility to medicines than other EU countries	PreIQ	85	3.61	.888	0.050
	PostIQM	86	3.36	.944	
The introduction of the unique identifier results in an increase in drug prices	PreIQ	85	3.58	.822	0.000
	PostIQM	86	2.99	1.057	

Table 3.28 shows that non-significant differences were present between the mean rating scores provided to statements in the PostIQM and PostIQB regarding the impact of the UI on accessibility to medicines and on drug prices. PostIQB participants agreed more with the first statement compared to PostIQM participants, while the opposite was true for the second statement.

Table 3.28: Comparison of Post-Implementation Questionnaire – Malta (PostIQM) (N=86) and Post-Implementation Questionnaire – Bonn (PostIQB) (N=17) Participants' Opinions Regarding UI Impact on Medicine Accessibility

		Sample size	Mean	Std. Dev.	P-value
The introduction of the unique identifier negatively impacts the accessibility of medicines	PostIQM	86	2.84	1.050	0.434
	PostIQB	17	3.00	.791	
The introduction of the unique identifier results in an increase in drug prices	PostIQM	86	2.99	1.057	0.068
	PostIQB	17	2.53	.514	

3.13 Impact of the UI on Workload

The majority of those who answered the PreIQ, PostIQM, and PostIQB strongly agreed or agreed that the UI significantly increased their workload (PreIQ: n=52; PostIQM: n=56; PostIQB: n=12). These results are shown in figure 3.8.

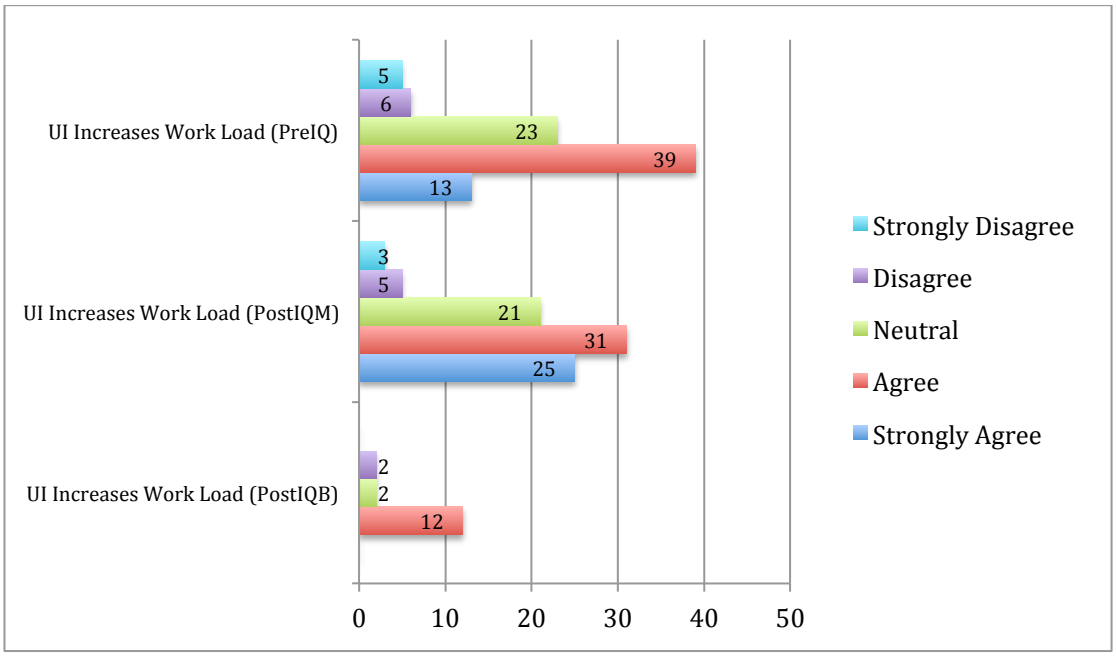

Figure 3.8: Number of Pharmacists in the PreIQ (N=85), PostIQM (N=86), and PostIQB (N=17) who Answered Strongly Agree, Agree, Neutral, Disagree, or Strongly Disagree to the Above Statement Regarding Impact of the UI on Work Load

Table 3.29 shows that a non-significant decrease was present in the mean rating score provided to the statement in the PreIQ and PostIQM regarding the impact of the UI on workload. This means that fewer PostIQM participants agreed with this statement compared to PreIQ participants.

Table 3.29: Comparison of Pre-Implementation Questionnaire (PreIQ) (N=85) and Post-Implementation Questionnaire-Malta (PostIQM) (N=86) Participants' Opinions Regarding UI Impact on Workload

		Sample size	Mean	Std. Dev.	P-value
The introduction of the unique identifier significantly increases your workload.	PreIQ	85	3.82	1.037	0.097
	PostIQM	86	3.57	1.024	

Table 3.30 shows that a non-significant difference was present in the mean rating score provided to the statement in the PostIQM and PostIQB regarding the impact of the UI on workload. This means that more PostIQB participants agreed with this statement compared to PostIQM participants.

Table 3.30: Comparison of Post-Implementation Questionnaire – Malta (PostIQM) (N=86) and Post-Implementation Questionnaire – Bonn (PostIQB) (N=17) Participants' Opinions Regarding UI Impact on Workload

		Sample size	Mean	Std. Dev.	P-value
The introduction of the unique identifier significantly increases your workload	PostIQM	86	3.57	1.024	0.958
	PostIQB	17	3.59	.712	

3.14 Use of the UI for the Direct Benefit of Patients

The majority of those who answered the PreIQ, PostIQM, and PostIQB strongly agreed or agreed that the UI can be used for the direct benefit of the patient (PreIQ: n=63; PostIQM: n=70; PostIQB: n=10). These results are shown in figure 3.9.

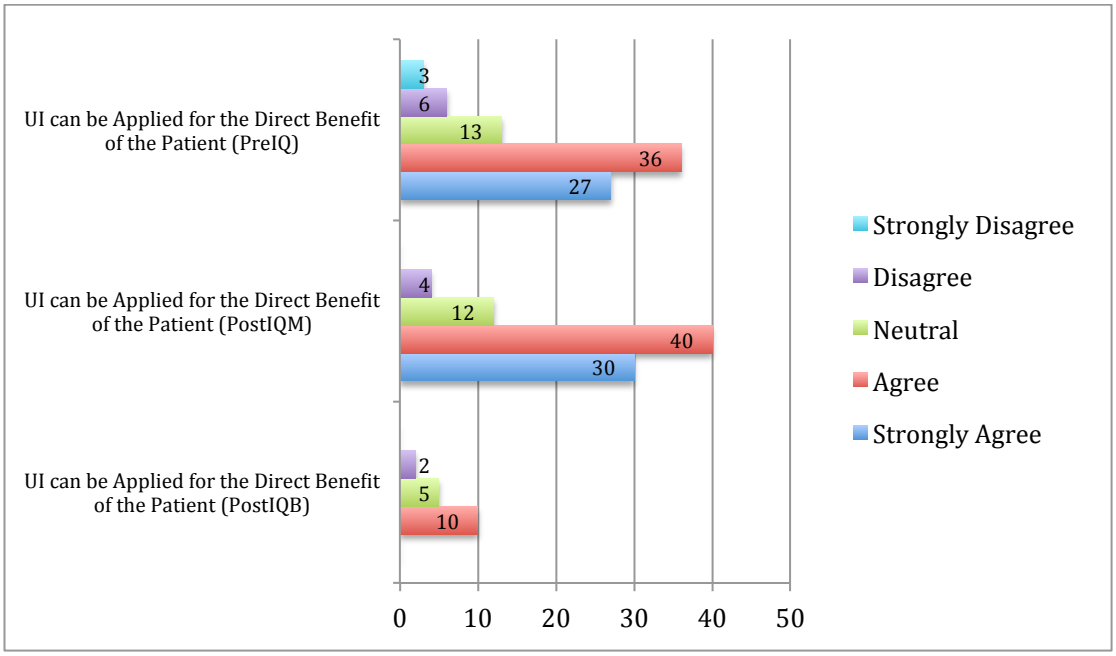

Figure 3.9: Number of Pharmacists in the PreIQ (N=85), PostIQM (N=86), and PostIQB (N=17) who Answered Strongly Agree, Agree, Neutral, Disagree, or Strongly Disagree to the Above Statement Regarding Use of the UI for Direct Patient Benefit

Table 3.31 shows that a non-significant increase was present in the mean rating score provided to the statement in the PreIQ and PostIQM regarding the use of the UI for the direct benefit of the patient. This means that more PostIQM participants agreed with this statement compared to PreIQ participants.

Table 3.31: Comparison of Pre-Implementation Questionnaire (PreIQ) (N=85) and Post-Implementation Questionnaire-Malta (PostIQM) (N=86) Participants' Opinions Regarding use of UI for the Direct Benefit of the Patient

		Sample size	Mean	Std. Dev.	P-value
The Falsified Medicines Directive can be applied for the direct benefit of the patient	PreIQ	85	3.92	1.038	0.321
	PostIQM	86	4.12	.818	

Table 3.32 shows that a significant difference was present in the mean rating score provided to the statement in the PostIQM and PostIQB regarding the use of the UI for the direct benefit of the patient. This means that fewer PostIQB participants agreed with this statement compared to PostIQM participants.

Table 3.32: Comparison of Post-Implementation Questionnaire – Malta (PostIQM) (N=86) and Post-Implementation Questionnaire – Bonn (PostIQB) (N=17) Participants' Opinions Regarding use of UI for the Direct Benefit of the Patient

		Sample size	Mean	Std. Dev.	P-value
The Falsified Medicines Directive can be applied for the direct benefit of the patient	PostIQM	86	4.12	.818	0.002
	PostIQB	17	3.47	.717	

3.15 Impact of Brexit and Covid-19 on the FMD

A focus group comprising of seven participants from different areas of expertise, including regulatory sciences (n=2), wholesale dealing (n=2), industrial pharmacy (n=1), and MaMVO (n=2), was held in order to explore the impact of Brexit and the Covid-19 pandemic on the FMD.

3.15.1 Challenges in Implementation and Compliance of the FMD

A number of points were brought up by participants regarding the difficulties encountered in implementation of and compliance with the FMD. These were:

- The small size of the island that made economies of scale difficult.
    - Expenses for setting up a repositories system were similar to those faced by larger countries, despite the small size of Malta.
- Problems faced by Malta as a small country, including geographical position, transportation, logistics, and low volume, were not highlighted during initial

discussion of the legislation with the EU commission.

  - Waivers such as the ones given to Greece and Italy were not granted to Malta due to these problems not being highlighted.

- Clerks had to be hired at CPSU in order to manually verify each pack.
- Inability to reverse decommissioning after ten days leads to increase in wastage.
- High fees associated with MaMVO membership for Marketing Authorisation Holders have led to increased registration of products under article 126a. This is due to fees applicable for article 126a authorisation holders being lower than fees applicable to marketing authorisation holders.
- Any products that were not in demand in Malta in high enough quantities were discontinued since third country manufacturers/wholesalers were not willing to serialize products unless a large number of packs were imported. In this case Malta's small market meant that importing the large quantities of packs required was unfeasible.
- Short period of implementation for manufacturers – Serialisation could not be rolled out slowly.
- Serialisation is not carried out by manufacturers in Malta – challenges associated with serialisation include low volume of products and costs involved.

3.15.2 Positive Aspects of the FMD

The main positive aspect identified by participants that was brought about by the implementation of the FMD was improvement in quality systems and decreased risk of falsified medicines entering the supply chain. Another positive aspect identified was that Malta managed to overcome the challenge of having little to no voice; this means that whenever new developments are discussed, the concerns of member states that have small markets, such as Malta, are also taken into account. It was also highlighted that most stakeholders are connected to MaMVO and it was observed that they are abiding by the rules.

3.15.3 Impact of Brexit on Stakeholders with respect to the FMD

Issues highlighted regarding the impact of Brexit were:

- The impact of Brexit on the National Health Service (NHS) and how to mitigate this impact has been studied extensively, but further work needs to be done.
- Malta's historical dependence on the UK market, its small market, and current lack of Maltese importers possessing the capability of affixing the safety features to medicinal packs, were all pointed out as Brexit related challenges faced by Malta. These vulnerabilities, along with the possibility that Malta may be slightly more lenient in granting batch specific exemptions permitting packs not bearing the safety features on the market due to this reliance on the UK market, may make Malta more vulnerable to the entry of falsified medicines into its legal supply chain.
    - It was also noted that despite this, wholesalers with years of experience

and a certain level of branding will be careful enough to only do business with reputable foreign suppliers, decreasing the risk that falsified medicines will penetrate the market, provided that all stakeholders are compliant.

- The grace period given to Italy and Greece means that there are difficulties in getting packs from these countries into the Maltese market – batch specific requests are submitted by wholesalers to the Licensing Authority in order for a product to be exempted from bearing the safety features.
- When article 126a products present on the Maltese market are scanned, an inter-market query is triggered with the UK repository. Since the UK repository is no longer viable due to Brexit, an alert is generated. This can be time-consuming for end users and those investigating these incidents.
- A European Commission notice exempts packs leaving the UK that are destined for markets that are historically dependent on the UK (Malta, Ireland, Northern Ireland, Cyprus) from being decommissioned (though they will still have to be verified). This was done because these markets lack the capability of affixing the safety features to medicinal packs.
    - It was noted that this exemption could increase Malta's exposure to falsified medicines. For this reason it was important to limit the number of exemptions made for Malta with respect to the FMD. An example given in this regard was of the issue of whether to end the stabilization period for pharmacies on the 9th of February 2021 or whether to extend it further while dealing with the fall-out from Brexit and Covid-19. In the end it was decided that this stabilization period should not be extended

in order to protect the legal supply chain from entry of falsified medicines.

- MaMVO was a key player in the risk assessment with respect to Brexit within EMVO. As such, Malta is very much involved in the feedback process on decisions made by the EU commission with respect to Brexit and the FMD, meaning that the concerns specific to Malta were taken into consideration.
    - Despite this, one key problem remains, this being that UK MAHs who choose to market only in the UK are not legally obliged to upload the UI to the repositories system. This is an issue for Malta since we are so dependent on the UK to maintain our healthcare system and ensure that medicines are available for patients.
- Brexit may worsen the financial impact of the FMD and UI in terms of the need for manufacturers and MAHs to start serializing products. This brings up concerns of low return on investment due to the low volume of products in the Maltese market, making serialisation a very expensive venture for Maltese manufacturers and MAHs.
    - It was further pointed out that manufacturers had already invested in serialisation software based on the current requirements, meaning that more investment would be required if a major update occurred. If the UK changes its serialisation requirements, manufacturers operating in the UK market could be required to invest in new software, update standard operating procedures (SOPs), retrain personnel, etc., all of which would be costly.

- Extensive use of batch specific exemptions resulting in a large number of packs being put on the market without the UI having been uploaded to the repositories system could be considered as non-compliance with Commission Delegated Regulation 2016/161, despite the fact that such batch specific exemptions are adequately provided for in the national legislation. In such a scenario, ensuring the continuity of supply of medication could be at the expense of full compliance with the FMD and Commission Delegated Regulation 2016/161.

3.15.4 Impact of Covid-19 on Stakeholders with respect to the FMD

The points put forward during the focus group regarding the impact of Covid-19 on FMD were analysed by means of a SWOT analysis.

3.15.4.1 Strengths

- Robust systems of importation and distribution of medicines in place.
- Covid-19 vaccines were exempted from bearing the safety features, therefore leading to a faster and more efficient delivery to patients.
- The risk of falsified Covid-19 vaccines entering the legal supply chain is currently mitigated by only allowing vaccines to be sent from the manufacturer directly to a government entity, who is responsible for the vaccines from the point at which the vaccines reach the island to the time that they are administered to patients.
- Covid-19 vaccine manufacturers have introduced tracking systems to make sure that each vaccine consignment ends up at the correct destination.

3.15.4.2 Weaknesses

- The high demand for Covid-19 vaccines, drugs being used for the management of Covid-19, and personal protective equipment, was identified as a weakness since this makes these vaccines a high target for counterfeiters.
- At the time of the focus group, the demand for Covid-19 vaccines was so high that manufacturers were not able to carry out serialisation of Covid-19 vaccines without decreasing production capacity, therefore causing a slower delivery to patients.

3.15.4.3 Opportunities

- Discussion of national legislation allowing for decommissioning of medicinal products by wholesalers in exceptional circumstances. This will allow more options regarding where and how Covid-19 vaccines are decommissioned.

3.15.4.4 Threats

- Allowing private importation of the vaccine. This can increase the risk of falsified Covid-19 vaccines entering the legal supply chain, especially if serialisation is not yet implemented.
- The exemption of Covid-19 vaccines from bearing the UI can also be considered a threat, as it increases the risk of falsified vaccines entering the legal supply chain.
- Uploading a large volume of serial numbers in the repositories system once serialisation of Covid-19 vaccines is implemented could overwhelm the system due to the large amounts of packs and corresponding serial numbers being

uploaded into the system.

- A large number of alerts can be generated when decommissioning Covid-19 vaccines due to double dispensing. This is because of the large amounts of Covid-19 vaccine vials within a single unit, which exceeds the limit for how many times a unit can be marked as dispensed. If this occurs, there is a risk that alerts generated will be ignored, impacting compliance.
- Drug shortages due to supply chain disruption may lead to patients using online pharmacies. This can lead to falsified medicines reaching patients if the online pharmacy used is unauthorized.

Chapter 4

Discussion

4.1 Study Outcomes

This study focused on the evaluating the envisaged impact of the UI from the point of view of pharmacists working in Malta before the implementation of the UI, the actual impact of the UI as experienced by pharmacists in Malta and Bonn, Germany, after the implementation of the UI, and how the impact of the UI as well as compliance with the FMD was further affected by Brexit and the Covid-19 pandemic.

4.1.1 Risk Posed by Falsified Medicines

Overall, participants in the PreIQ, PostIQM, and PostIQB agreed that falsified medicines are a problem in the EU and that the UI is a positive and proportional tool for preventing their entry into the legal supply chain. Nevertheless there was a significant decrease in participants who agreed that the introduction of the UI significantly reduced the entry of falsified medicines within the Legal Supply Chain in the PostIQM compared to the PreIQ. Moreover, the number of participants who reported encountering cases of falsified medicines almost doubled in the PostIQM when compared to the PreIQ, even though this difference was not found to be significant.

Brexit and Covid-19 also further complicate the scenario, as both can increase the risk of falsified medicines entering the legal supply chain, since exemptions granted to mitigate the fall-out from Brexit and Covid-19 can be exploited by counterfeiters.

4.1.2 Financial Impact

While participants may have agreed about the usefulness of the UI in preventing falsified medicines from entering the supply chain, the majority of participants in all three questionnaires did not agree that the UI is worth its financial impact. Brexit can also worsen the financial impact of the UI since wholesalers and manufacturers may be forced to start serialisation, despite Malta having a small and low-volume market, which limits the possible return on investment. It should also be noted that this would not impact compliance with the FMD since any money spent on implementing serialisation would be with the goal of being compliant with the FMD in the first place.

4.1.3 Impact on Medicine Accessibility

The majority of participants in the PreIQ, PostIQM, and PostIQB, did not agree that UI implementation would negatively impact accessibility to medicines. In the PreIQ, a majority of participants agreed that drug prices would increase as a result of UI introduction, but the PostIQM participants who agreed with this statement decreased significantly, while none of the PostIQB participants agreed that the UI had caused drug prices to increase. The same was true about whether Malta would be hit harder by UI introduction due to its reliance on 126a products, parallel trade, and SMEs, with the majority agreeing in the PreIQ but a significant decrease in agreement amongst participants in the PostIQM.

Ensuring fast delivery of and accessibility to Covid-19 vaccines is also of great importance. This lead to Covid-19 vaccines being temporary exempted from bearing the UI, which may have increased the risk of falsified Covid-19 vaccines entering the

legal supply chain. This risk is decreased since Covid-19 vaccines are currently being transported from the manufacturer directly to a government entity that is responsible for the vaccines until they are administered to patients. Since this distribution process involves less intermediaries, the points at which falsified vaccines may enter the legal supply chain decreases.

Brexit also had a large impact on accessibility to medicines in Malta due to the historical dependence on the UK market and the large amount of drugs registered under Article 126a linked to marketing authorisation holders in the UK. Exemptions granted to Italy and Greece from implementation of the safety features further impacted medicine accessibility in Malta. While the FMD itself may not have impacted accessibility and drug prices significantly, Brexit worsened its impact.

It should also be noted that drug shortages might increase the use of online pharmacies. This may increase the risk of falsified drugs reaching patients if unauthorized sellers are used. For this reason, education of the public regarding the risks associated with falsified medicines, as well as ways to recognize legitimate online pharmacies from those operating without a license, is of utmost importance.

4.1.4 Impact on Work Load

The majority of participants in the PreIQ, PostIQM, and PostIQB agreed that the UI would increase the number of man-hours required per week and that the UI would increase their workload. In the PreIQ, the majority of participants estimated that the increase in man-hours would be of 10 hours per week, but in both the PostIQM and the PostIQB the majority stated that the increase had been of 5 hours per week. This shows that before the implementation of the UI participants may have overestimated

the workload involved.

4.2 Study Limitations

The main limitations of this study included the small sample sizes for the questionnaires as well as the limited time available for discussion during the focus group.

Pharmacists in Bonn were sometimes unable to answer the questionnaire due to the language barrier and time constraints. All the participants in Bonn were also community pharmacists, meaning that the evaluation of the impact of the UI in Bonn is based only on the experience of members of one pharmaceutical sector rather than pharmacists from different work backgrounds.

As a result of the Covid-19 pandemic, the PostIQM could not be physically disseminated in community pharmacies, as was done with the PreIQ and PostIQB. This is due to social distancing measures and internal paperless policies adopted by community pharmacies in Malta.

Due to the nature of focus groups as a research technique, a very limited time was available during which discussion could take place. This meant that a number of potential topics could not be discussed due to the time limit. It should also be noted that conducting only one focus group session limited the findings of the focus group to only what was known at the time of discussion, therefore not fully addressing the fluidity of the situation surrounding Brexit and Covid-19.

4.3 Recommendations

One of the strengths of this study was in its inclusion of pharmacists from different work backgrounds in the PreIQ and PostIQM, with most of the participants recruited

being hospital pharmacists and community pharmacists. An improvement would be to include more participants from industrial pharmacy, wholesale dealing, and regulatory science. It might also be useful to include in the study other workers from the pharmaceutical sector, such as pharmaceutical technologists and technicians, whose work was also impacted by the FMD and the introduction of the UI.

It is also recommended that several focus group sessions take place over a number of months. This would enable the discussion of a broader range of topics as well as take into account any developments in the ever-changing scenarios of Brexit and Covid-19 over a longer time period.

4.4 Conclusion

Results indicate that overall, the introduction of FMD and the UI are seen by pharmacists and pharmaceutical stakeholders in a positive light, even if their financial impact may be worrisome. While the Falsified Medicines Directive may make the challenges posed by Brexit and Covid-19 greater, the unique identifier and the anti-tampering device, as well as compliance with the Falsified Medicines Directive, should also be regarded as an integral part of the medicinal product rather than a challenge to be overcome.

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Appendices

Appendix 1: Ethics Approval

FACULTY RESEARCH ETHICS COMMITTEE <research-ethics.ms@u... Fri, 18 Dec 2020, 10:54

to me

Dear Ms Debono,

Since your self-assessment resulted in no issues being identified, FREC will file your application for record and audit purposes but will not review it.

Any ethical and legal issues including data protection issues are your responsibility and that of your supervisor.

Kindly confirm that you sent all the documents which you attached to the UREC form and also other documents related to your study for audit purposes.

•••

L-Università ta' Malta

Ruth Stivala | Secretary
B.A.(Hons)(Melit.),M.A.(Melit.)

Faculty Research Ethics Committee
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Medical School, Mater Dei Hospital
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Appendix 2: Focus Group Consent Form – Questionnaire Development and Validation

Informed Consent Form

Student: Mireille Debono (mireille.debono.15@um.edu.mt)
Principal Supervisor: Professor Anthony Serracino Inglott
Co-Supervisor: Dr. Nicolette Sammut Bartolo

Purpose

This study investigates the opinions of those working in different pharmaceutical fields on the impact of the unique identifier on accessibility, dispensing, and distribution of medicines in Malta. As part of this study you will be asked to participate in a focus group.

Participant's Rights

I understand that my responses will be kept in the strictest of confidence. Data collected is anonymous and no one will be able to identify me when the results are reported and my name will not appear anywhere in the written report. I will not share other participants' identities or opinions from the discussion with others so as to maintain the anonymity of all the participants.

I also understand that I may skip any questions that I do not wish to answer and that I may withdraw from the study at any time without any explanation being required or any negative consequence for the individual. These consent forms will be kept separate from the data records in order to ensure anonymity. I understand that my verbal responses will be recorded and transcribed for further analysis.

I was informed about my rights to access, rectify, and where applicable erase the data concerning me

I understand that I am participating in this study of my own free will.

Consent to Participate

I acknowledge that I am at least eighteen years old, and that I understand my rights as a research participant as outlined above. I acknowledge that my participation is strictly voluntary.

Print Name:_____

Participant Signature:_____
Date:_____

Signature of Principal Supervisor:_____

Signature of Researcher:_____

Appendix 3: Focus Group Question Sheet - Questionnaire Development and Validation

Focus Group on the Impact of Unique Identifier on Drug Products

Introduction *(for use by moderator)*

Welcome and thank you for accepting to invitation to participate in this focus group.

This focus group is being organised as part of my dissertation and the objective is to take a look at the impact of the Unique Identifier on drug products. The results of this focus group will then be used to develop a questionnaire.

You were selected because all of you are in some way impacted by the implementation of the unique identifier.

As moderator I will be guiding the conversation.

This session will be recorded and then transcribed for further analysis.

Ground Rules *(for use by moderator)*

Remember that there are no wrong answers just different opinions.

Speak one at a time.

Keep focused on the topic at hand.

General opening questions *(for use by moderator)*

Are falsified medicines a significant problem in the EU/Malta?

Will the introduction of the UI significantly decrease the entry of falsified medicines into the legal supply chain?

Awareness regarding the UI *(for use by moderator)*

Do you think there is enough information available for patients and pharmacists regarding the UI?

Impact on Workload of UI *(for use by moderator)*

What kind of impact will the UI have on your day to day activities at work?

Financial Impact of UI *(for use by moderator)*

What kind of financial impact will the UI have on different pharmaceutical sectors. Will this added expense be worth any potential advantages that the UI might have?

Impact of UI on Access to Medicines (*for use by moderator)*

Does the introduction of the UI carry a risk of drug shortages occurring?

Can drug prices increase after the UI is introduced?

Miscellaneous *(for use by moderator)*

What is your opinion on the exclusion of OTC drugs from bearing the UI?

At which point should National Health Service medicines be decommissioned?

Closing Questions (*for use by moderator)*

Any other comments?

Appendix 4: Pre-Implementation Questionnaire

The Unique Identifier on Drug Products: Questionnaire

Student: Mireille Debono
Email address: mireille.debono.15@um.edu.mt
Contact number: 79800464

Principal Supervisor: Professor Anthony Serracino Inglott
Email address: anthony.serracino-inglott@um.edu.mt
Contact number: 23402901

Dear Sir/Madam,

I am currently reading for a Bachelor of Science in Pharmaceutical Science at the University of Malta. As part of my dissertation I am conducting a study among those working in different pharmaceutical fields to determine their views on the impact of the Unique Identifier on dispensing, distribution and accessibility of medicines in Malta. This study is being conducted under the supervision of Professor Anthony Serracino Inglott and the co-supervision of Dr. Nicolette Sammut Bartolo.

The data collected will not identify the participant, as it will be anonymous. The findings from this study may be disseminated and published e.g. oral and poster presentations, and published in the medical and scientific arenas.

Participation is strictly on a voluntary basis and participants may withdraw from the study at any time without any need for explanation. By answering this questionnaire, you are giving your consent to participate.

Your time and participation is greatly appreciated. If you have any questions regarding the study please contact me on mireille.debono.15@um.edu.mt.

Best Regards,

Mireille Debono

The Unique Identifier on Drug Products: Questionnaire

Demographics

1) Age:_____

2) Gender:

- Male
- Female
- Other:_____

3) Work Sector:

- Hospital Pharmacy
- Community Pharmacy
- Wholesale dealing
- Regulatory Sciences
- Industrial Pharmacy
- Other:_____

4) Years of Experience:

- 1-10 years
- 11-20 years
- 21-30 years
- >30 years

5) Job Position:_____

Falsified Medicines and the Unique Identifier

6) Have you ever encountered a case of medicine falsification during your practice?

- o Yes
- o No

7) How did you first hear about the introduction of the unique identifier?

- o Official correspondence
- o Colleagues
- o Social media
- o Mass media (e.g. Internet, TV, Radio, etc.)
- o Other:_____

If though official correspondence, please specify:

_____

8) When did you first hear about the introduction of the unique identifier?

- o In the past month
- o In the past year
- o Before 2018
- o Other:_____

9) Are you aware of the components of the unique identifier?

- o Yes
- o No

If Yes, which of the following are components of the unique identifier?

- o An alphanumeric/numeric serial number
- o The batch number
- o The EU registration number
- o The expiry date
- o The national reimbursement number
- o The product code

10) Are you aware of the function of the unique identifier?

- Yes
- No

If Yes can you describe the function of the unique identifier?

_____
_____
_____

For the purposes of the next question 'decommissioning of the unique identifier' refers to the action by which the active status of a unique identifier is converted to a status in which it cannot be successfully verified or authenticated.[1]

11) At which point should decommissioning take place for National Health Service medication in a hospital or pharmacy setting?

- Before being transported to the hospital/ community pharmacy
- Upon arrival at the hospital/ community pharmacy
- Just before being dispensed by the pharmacist
- Other:_____

12) Do you agree with the decision by the EU to exclude OTC products from bearing the unique identifier?

- Yes
- No

Why?_____

[1]European Commission. 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 [Internet]. Official Journal of the European Union. 2016; L32:1-27 [cited 2019 Jan 2]. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0161&from=EN

13) Should Malta have been exempted from introducing the unique identifier?

- Yes
- No

Why?_____

14) Has the introduction of the unique identifier resulted in more man hours being required?

- Yes
- No

If Yes, how many additional man hours were required per week?

- 5
- 10
- 20
- 30
- >30

15) Kindly rate the following statements related to the introduction of the unique identifier and falsified medicines from strongly agree to strongly disagree.

	Strongly Agree	**Agree**	**Neutral**	**Disagree**	**Strongly Disagree**
Entry of falsified medicines into the legal supply chain is a significant problem in EU countries					
The introduction of the unique identifier resulted in a significant decrease in the entry of falsified medicines within the Legal Supply Chain.					
The introduction of the unique identifier is a proportional response to the problem of falsified medicines in EU countries					
You had enough time to prepare for the introduction of the unique identifier					

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
There is enough information available for pharmacists about the unique identifier					
There is enough information available for patients about the unique identifier					
Any potential benefits of the unique identifier are worth the financial impact it may have had on your sector					
The introduction of the unique identifier will attract more pharmaceutical companies to invest in Malta					
The introduction of the unique identifier will allow pharmaceutical companies to increase their profits in the long run					

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
The immediate financial impact posed by the introduction of the unique identifier was risky for the Maltese market					
The introduction of the unique identifier caused a significant amount money to be saved due to less hospitalizations as a direct result of intake of fake drugs					
The introduction of the unique identifier has significantly increased your work load					
The introduction of the unique identifier has negatively impacted accessibility of medicines in Malta					

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
Malta's dependence on 126(a) products, parallel trade products and small and medium enterprises means that it will be hit harder with respect to medicines than other EU countries					
The introduction of the unique identifier has resulted in an increase in drug prices					
The Falsified Medicines Directive can be applied for the direct benefit of the patient					

Appendix 5: Post-Implementation Questionnaire - Malta

The Unique Identifier on Drug Products: Questionnaire

Student: Mireille Debono
Email address: mireille.debono.15@um.edu.mt
Contact number: 79800464

Principal Supervisor: Professor Anthony Serracino Inglott
Email address: anthony.serracino-inglott@um.edu.mt
Contact number: 23402901

Dear Sir/Madam,

I am currently reading for a Bachelor of Science in Pharmaceutical Science at the University of Malta. As part of my dissertation I am conducting a study among those working in different pharmaceutical fields to determine their views on the impact of the Unique Identifier on dispensing, distribution and accessibility of medicines in Malta. This study is being conducted under the supervision of Professor Anthony Serracino Inglott and the co-supervision of Dr. Nicolette Sammut Bartolo.

The data collected will not identify the participant, as it will be anonymous. The findings from this study may be disseminated and published e.g. oral and poster presentations, and published in the medical and scientific arenas.

Participation is strictly on a voluntary basis and participants may withdraw from the study at any time without any need for explanation. By answering this questionnaire, you are giving your consent to participate.

Your time and participation is greatly appreciated. If you have any questions regarding the study please contact me on mireille.debono.15@um.edu.mt.

Best Regards,

Mireille Debono

The Unique Identifier on Drug Products: Questionnaire

Demographics

1) Age:_____

2) Gender:

- Male
- Female
- Other:_____

3) Work Sector:

- Hospital Pharmacy
- Community Pharmacy
- Wholesale dealing
- Regulatory Sciences
- Industrial Pharmacy
- Other:_____

4) Years of Experience:

- 1-10 years
- 11-20 years
- 21-30 years
- >30 years

5) Job Position:_____

Falsified Medicines and the Unique Identifier

6) Have you ever encountered a case of medicine falsification during your practice?

- Yes
- No

7) How did you first hear about the introduction of the unique identifier?

- Official correspondence
- Colleagues
- Social media
- Mass media (e.g. Internet, TV, Radio, etc.)
- Other:_____

If through official correspondence, please specify:

_____

8) When did you first hear about the introduction of the unique identifier?

- In the past year
- In 2018
- Before 2018
- Other:_____

9) Are you aware of the components of the unique identifier?

- Yes
- No

If Yes, which of the following are components of the unique identifier?

- An alphanumeric/numeric serial number
- The batch number
- The EU registration number
- The expiry date
- The national reimbursement number
- The product code

10) Are you aware of the function of the unique identifier?

- Yes
- No

If Yes can you describe the function of the unique identifier?

_____
_____
_____

11) At which point should decommissioning take place for National Health Service medication in a hospital or pharmacy setting?

- Before being transported to the hospital/ community pharmacy
- Upon arrival at the hospital/ community pharmacy
- Just before being dispensed by the pharmacist
- Other:_____

12) Do you agree with the decision by the EU to exclude OTC products from bearing the unique identifier?

- Yes
- No

Why?_____

13) Should Malta have been exempted from introducing the unique identifier?

- Yes
- No

Why?_____

14) Has the introduction of the unique identifier resulted in more man hours being required?

- Yes
- No

If Yes, how many additional man hours were required per week?

- 5
- 10
- 20
- 30
- >30

15) Kindly rate the following statements related to the introduction of the unique identifier and falsified medicines from strongly agree to strongly disagree.

	Strongly Agree	**Agree**	**Neutral**	**Disagree**	**Strongly Disagree**
Entry of falsified medicines into the legal supply chain is a significant problem in EU countries					
The introduction of the unique identifier resulted in a significant decrease in the entry of falsified medicines within the Legal Supply Chain					
The introduction of the unique identifier is a proportional response to the problem of falsified medicines in EU countries					

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
You had enough time to prepare for the introduction of the unique identifier					
There is enough information available for pharmacists about the unique identifier					
There is enough information available for patients about the unique identifier					
Any potential benefits of the unique identifier are worth the financial impact it may have had on your sector					
The introduction of the unique identifier will attract more investment by pharmaceutical companies					
The introduction of the unique identifier will allow pharmaceutical companies to increase their profits in the long run					

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
The immediate financial impact posed by the introduction of the unique identifier was risky for the Malta/EU market					
The introduction of the unique identifier caused a significant amount of money to be saved due to less hospitalizations as a direct result of intake of fake drugs					
The introduction of the unique identifier has significantly increased your work load					
Malta's dependence on 126(a) products, parallel trade products and small and medium enterprises means that it has been hit harder with respect to accessibility to medicines than other EU countries					

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
The introduction of the unique identifier has negatively impacted accessibility to medicines					
The introduction of the unique identifier has resulted in an increase in drug prices					
The Falsified Medicines Directive can be applied for the direct benefit of the patient					

16) Any other comments you may wish to add?

_____
_____
_____

Appendix 6: Post-Implementation Questionnaire – Bonn

The Unique Identifier on Drug Products: Questionnaire

Student: Mireille Debono
Email address: mireille.debono.15@um.edu.mt
Contact number: 79800464

Principal Supervisor: Professor Anthony Serracino Inglott
Email address: anthony.serracino-inglott@um.edu.mt
Contact number: 23402901

Dear Sir/Madam,

I am currently reading for a Bachelor of Science in Pharmaceutical Science at the University of Malta. As part of my dissertation I am conducting a study among those working in different pharmaceutical fields to determine their views on the impact of the Unique Identifier on dispensing, distribution and accessibility of medicines in Malta. This study is being conducted under the supervision of Professor Anthony Serracino Inglott and the co-supervision of Dr. Nicolette Sammut Bartolo.

The data collected will not identify the participant, as it will be anonymous. The findings from this study may be disseminated and published e.g. oral and poster presentations, and published in the medical and scientific arenas.

Participation is strictly on a voluntary basis and participants may withdraw from the study at any time without any need for explanation. By answering this questionnaire, you are giving your consent to participate.

Your time and participation is greatly appreciated. If you have any questions regarding the study please contact me on mireille.debono.15@um.edu.mt.

Best Regards,

Mireille Debono

The Unique Identifier on Drug Products: Questionnaire

Demographics

1) Age:_____

2) Gender:

- Male
- Female
- Other:_____

3) Work Sector:

- Hospital Pharmacy
- Community Pharmacy
- Wholesale dealing
- Regulatory Sciences
- Industrial Pharmacy
- Other:_____

4) Years of Experience:

- 1-10 years
- 11-20 years
- 21-30 years
- >30 years

5) Job Position:_____

Falsified Medicines and the Unique Identifier

6) Have you ever encountered a case of medicine falsification during your practice?

- o Yes
- o No

7) How did you first hear about the introduction of the unique identifier?

- o Official correspondence
- o Colleagues
- o Social media
- o Mass media (e.g. Internet, TV, Radio, etc.)
- o Other:_____

If though official correspondence, please specify:

_____

8) When did you first hear about the introduction of the unique identifier?

- o In the past month
- o In the past year
- o Before 2018
- o Other:_____

9) Are you aware of the components of the unique identifier?

- o Yes
- o No

If Yes, which of the following are components of the unique identifier?

- o An alphanumeric/numeric serial number
- o The batch number
- o The EU registration number
- o The expiry date
- o The national reimbursement number
- o The product code

10) Are you aware of the function of the unique identifier?

- Yes
- No

If Yes can you describe the function of the unique identifier?

_____
_____
_____

11) At which point should decommissioning take place for National Health Service medication in a hospital or pharmacy setting?

- Before being transported to the hospital/ community pharmacy
- Upon arrival at the hospital/ community pharmacy
- Just before being dispensed by the pharmacist
- Other:_____

12) Do you agree with the decision by the EU to exclude OTC products from bearing the unique identifier?

- Yes
- No

Why?_____

13) Should there be exemptions from introducing the unique identifier?

- Yes
- No

Why?_____

14) Has the introduction of the unique identifier resulted in more man hours being required?

- Yes
- No

If Yes, how many additional man hours were required per week?

- 5
- 10
- 20
- 30
- >30

15) Kindly rate the following statements related to the introduction of the unique identifier and falsified medicines from strongly agree to strongly disagree.

	Strongly Agree	**Agree**	**Neutral**	**Disagree**	**Strongly Disagree**
Entry of falsified medicines into the legal supply chain is a significant problem in EU countries					
The introduction of the unique identifier resulted in a significant decrease in the entry of falsified medicines within the Legal Supply Chain.					
The introduction of the unique identifier is a proportional response to the problem of falsified medicines in EU countries					

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
You had enough time to prepare for the introduction of the unique identifier					
There is enough information available for pharmacists about the unique identifier					
There is enough information available for patients about the unique identifier					
Any potential benefits of the unique identifier are worth the financial impact it may have had on your sector					
The introduction of the unique identifier will attract more investment by pharmaceutical companies.					
The introduction of the unique identifier will allow pharmaceutical companies to increase their profits in the long run					

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
The immediate financial impact posed by the introduction of the unique identifier was risky for the German/EU market					
The introduction of the unique identifier caused a significant amount money to be saved due to less hospitalizations as a direct result of intake of fake drugs					
The introduction of the unique identifier has significantly increased your work load					
The introduction of the unique identifier has negatively impacted accessibility of medicines					
The introduction of the unique identifier has resulted in an increase in drug prices					

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
The Falsified Medicines Directive can be applied for the direct benefit of the patient					

16) Any other comments you may wish to add?

_____
_____
_____

Appendix 7: Focus Group Consent Form – Impact of Brexit and Covid-19 on Compliance with the Falsified Medicines Directive

Informed Consent Form

Student: Mireille Debono (mireille.debono.15@um.edu.mt)
Principal Supervisor: Professor Anthony Serracino Inglott
Co-Supervisor: Dr. Nicolette Sammut Bartolo

Purpose

This study investigates the opinions of a number of professionals on the impact of Brexit and Covid-19 on compliance with the Falsified Medicines Directive. As part of this study you will be asked to participate in a focus group.

Participant's Rights

I understand that my responses will be kept in the strictest of confidence. Data collected is anonymous, no one will be able to identify me when the results are reported and my name will not appear anywhere in the written report. I will not share other participants' identities or opinions from the discussion with others so as to maintain the anonymity of all the participants.

I also understand that I may skip any questions that I do not wish to answer and that I may withdraw from the study at any time without any explanation being required or any negative consequence for the individual. These consent forms will be kept separate from the data records in order to ensure anonymity. I understand that my verbal responses will be recorded and transcribed for further analysis.

I was informed about my rights to access, rectify, and where applicable erase the data concerning me

I understand that I am participating in this study of my own free will.

Consent to Participate

I acknowledge that I am at least eighteen years old, and that I understand my rights as a research participant as outlined above. I acknowledge that my participation is strictly voluntary.

Print Name:_____

Participant Signature:_____
Date:_____

Signature of Principal Supervisor:_____

Signature of Researcher:_____

Appendix 8: Focus Group Question Sheet - Impact of Brexit and Covid-19 on Compliance with the Falsified Medicines Directive

Focus Group on the Impact of Brexit and the Covid-19 Pandemic on Compliance with the Falsified Medicines Directive

Introduction *(for use by moderator)*

Welcome and thank you for accepting to invitation to participate in this focus group.

This focus group is being organised as part of my MPharm dissertation and the objective is to take a look at the impact of Brexit and Covid-19 on compliance with the Falsified Medicines Directive.

You were selected because all of you were in some way involved in the implementation of the unique identifier and the Falsified Medicines Directive.

As moderator I will be guiding the conversation.

This session will be recorded and then transcribed for further analysis.

Ground Rules *(for use by moderator)*

Remember that there are no wrong answers just different opinions.

Speak one at a time.

Keep focused on the topic at hand.

General opening questions *(for use by moderator)*

What were the difficulties encountered in implementing the FMD and compliance with FMD observed from a wholesale dealing/Regulatory/industry/inspectorate perspective

What were the positive of FMD on your sector?

Brexit *(for use by moderator)*

The FMD and the rules laid out in Delegated Regulation 2016/161 have ceased to apply in the UK as of 31st December 2020. How does this impact stakeholders in Malta?

- Might this cause a financial burden and if yes how may this impact compliance?
- Might this worsen the Out of Stock (OOS) situation expected to occur as a result of Brexit?

- Might this increase the risk of falsified medicines entering the Maltese supply chain?

Covid-19 ***(for use by moderator)***

Covid-19 Vaccine (*for use by moderator)*

Can Covid-19 vaccines be a target for counterfeiters?

Can Covid-19 vaccines bearing the UI and ATD slow down distribution of the vaccines throughout the EU?

Should Covid-19 vaccines be exempted from bearing the UI/ATD? How will this impact risk of falsification of Covid-19 vaccines?

Internet Pharmacies and Covid-19/Brexit ***(for use by moderator)***

Can OOS situation due to Brexit and social distancing/quarantine drive people to buy drugs from Internet pharmacies?

Are patients aware of the logo that certifies an Internet pharmacy as genuine?

Are patients aware of the risk of falsified medicines when buying drugs from online sources?

Is there a possibility of an online pharmacy being set up in Malta?

Closing Questions ***(for use by moderator)***

Any other comments?