Cost Evaluation Falsified Medicines Directive

Impact for manufacturers of generic medicines in the Netherlands

Commissioned by Bogin

Utrecht, november 2017

Capgemini Consulting

BOGIN

Contents

Executive summary

Cost Evaluation Falsified Medicine Directive

Context	To counteract falsified medicinal products for human use in the European market, the European Commission agreed with the 'Falsified Medicines Directive' (FMD) in 2016. As of February 9, 2019, the prescription drug packages will have to be marked with an anti-tampering device and a unique serial number, which will be registered in a European and national databank. This new regulation is expected to have significant impact on the costs of generic medicinal products in the Netherlands.
Objective	At the request of Bogin, the Dutch Generic and Biosimilar Medicines Association, the additional costs of the FMD are investigated for the Dutch market.
Findings	The additional costs of the FMD for the Dutch manufacturers of generic medicines are estimated at an average of € 0,17 per packaging. These additional costs relate to the adjustment of packaging lines. Extra units are added to the packaging lines in order to apply the anti-tampering device and data matrix that includes the unique serial number. Moreover, additional costs also arise as a result of software customization and efficiency loss due to delay of lines and more losses and controls in the packaging process. Furthermore, important (internal and external) additional costs are linked to the exchange of the unique serial numbers with the European and national databank. The additional costs per generic medicine packaging vary to a great extent; this depends on the volume at which a manufacturer offers a medicine in its completeness on the market.
Impact	Manufacturers of generic medicines in the Netherlands offer their products against (internationally) low costs, with low margins on the market. When the costs of the FMD are not passed on in the market price, this could have serious implications for the availability of these medicines in the Dutch market.

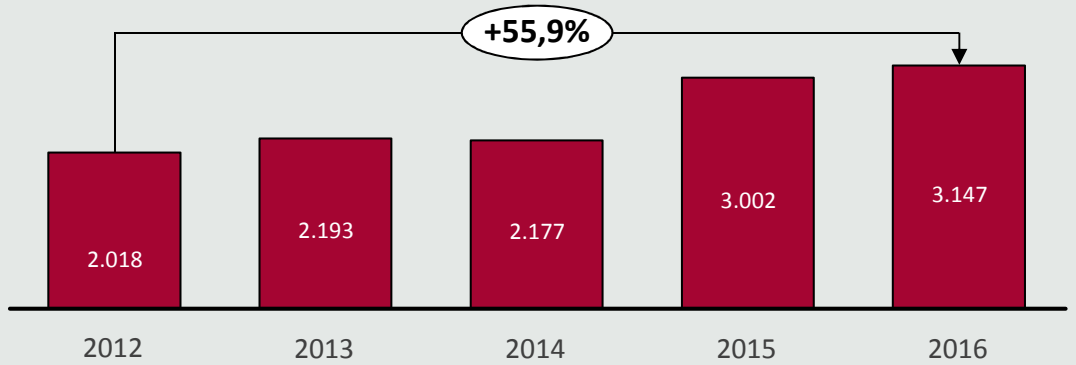
1. Introduction

In 2016, the European Commission of Falsified Medicines Directive (FMD) stated the following: As from 9 February 2019 onwards, all European countries should have a National Medicines Verification System (NMVS). The various partners in the pharmaceutical supply chain i.e. manufacturer, parallel importer, wholesaler, pharmacist and the government make sure that with this system, outer packaging (or secondary packaging) of prescription-only medicines, all have a valid serial number and anti-tampering device (such as a seal).

The FMD was established as a result of a worldwide increase of incidents with counterfeit medicines (see figure 1). The actual number of frauds is estimated to be higher. Indeed, pharmacists, physicians and patients cannot see with the naked eye whether the prescribed medicine has a wrong dosage or non-active components that are poisoned. Counterfeit medicines are often offered through the internet illegally; it is important that these medicines do not end up with patients through legal supply channels. With the mandatory verification of the serial number (serialisation) and the anti-tampering device, the European Union - as well as many other non EU-countries – have taken measures to maintain safety of patients on individual levels.

Manufacturers and parallel importers have an important responsibility in every National Medicine Verification system. Besides taking care of the appropriate packaging and registration of serial numbers, they carry the costs for the NMVS and the related European databank (EMVS) through their Marketing Authorisation Holders.

Figure 1 – Incidents with counterfeit medicines



Source: Pharmaceutical Security Institute (2017)

2. Problem definition en outline

2.1 Problem definition

In the Netherlands, almost three quarter of the prescription-only medicines are delivered by manufacturers of generic medicines. Since generic medicines are significantly cheaper than innovative medicines, the revenues of generic medicines are only 17% of the total pharmaceutical costs in the extramural pharmacy*.

Bogin, the Dutch Generic and Biosimilar Medicines Association**, assumes that the implementation of the FMD will create substantial costs for manufacturers. When considering the low margins on generic medicines, these costs cannot not be absorbed. Bogin expects that not providing an adequate compensation for the additional costs could have considerable implications for the availability of the generic medicines in the Dutch market.

Bogin, the Dutch Ministry of Health and the health insurers are in further consultation on this matter. To gain insight into the additional costs of Dutch generic medicine manufacturers as a result of the FMD, Bogin has asked Capgemini Consulting to investigate this matter.

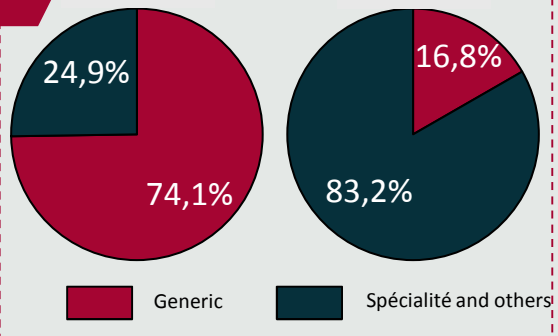
2.2 Outline

This report describes the results of the cost evaluation FMD at Dutch generic medicine manufacturers. The research was conducted in the period of August to October 2017. Chapter 3 explains the approach and limitations of the research. Chapter 4 provides a rough calculation of the additional costs as a consequence of the FMD for Dutch generic medicine manufacturers. Moreover, chapter 5 outlines the generic medicine market and FMD's impact, based on the study findings. Finally, chapter 6 presents the conclusions of this research study.

Generic Medicines

Generic medicines are the therapeutic equivalent of an original pharmaceutical product, a so-called innovative medicines. Generic medicines can be offered in the market once the patent of the innovative product has expired and it has been indicated that the generic medicine has the same effect as the original.

Volume **Costs**



Generic products are responsible for 74% of the medical provisions and 16,8% of he costs of extramural pharmacy in the Netherlands.

Source: Stichting Farmaceutische Kengetallen (2016; 2017)

* Generic medicines are also deployed in hospitals and other healthcare facilities.
** Bogin has 8 member who represent roughly 90% of the generic market in the Netherlands (see www.bogin.nl).

3. Research approach

Research steps:

Firstly, international research publications on FMD and the implications for the various manufacturers were studied (see appendix B for an overview). No recent (international) studies on the costs of FMD for manufacturers were found. However, the European Union has drawn up an overview of the estimated costs that are expected to occur as a result of the FMD. The results of this are discussed in chapter 4.

Secondly, the research focused on generating data on costs that are related with the FMD at manufacturers of generic medicines. With the help of a priory drawn up overview of potential costs and benefits parameters, a great deal of data was collected. In total, 7 interviews were conducted with manufacturers (4), contract packers of medicines (2) and the NMVO (1). Although willingness to cooperate was great, justification of the costs appeared to be a challenge. The implementation of the FMD is still in its preparation phase. Part of the costs that will arise are known. For other costs an estimation was made, which is partly based on established experiences elsewhere. In chapter 4 and appendix C, the calculations for every cost category are discussed.

The third step involved the collection of quantitative data on the scale of generic prescription-only medicines in the Netherlands. For this purpose, available data from national databanks and research institutes were collected. This resulted in an estimation of the additional costs of the FMD in total and per packaging for the manufacturers of generic medicine and the corresponding bandwidths (chapter 5).

The (interim) results of the cost evaluation are shared and tested with a guidance committee, with representatives of Bogin, the Dutch Ministry (listener), the Dutch Association of Innovative Medicine and a contract packer took part (see appendix A). The comments of the guidance committee members were taken into consideration during the development of this report.

4. FMD and financial implications for the manufacturers of generic medicines

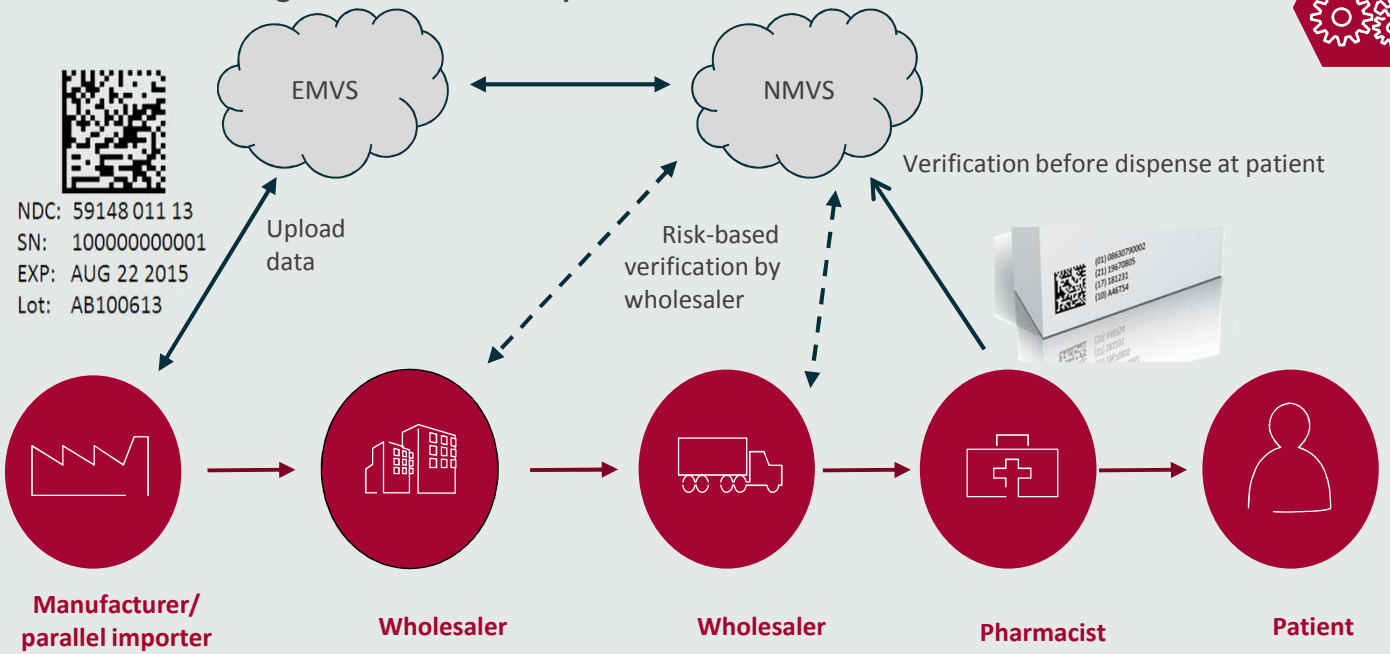
4.1 What does the Falsified Medicines Directive (FMD) mean for manufacturers?

As of February 9 2019, the Falsified Medicines Directive (FMD) requires all European countries to comply with two important guidelines:

1. All European countries are required to set up a National Medicine System (NMVS). De manufacturers and their Marketing Authorisation Holders (MAH's) took the initiative, as stated in the FMD, to set up jointly with other chain partners and the government a NMVS in every country, and therefore carry the costs. At the same time, on account of the European association of manufacturers and other chain partners a European Medicine Verification System (EMVS) was established. Through the European and national system, the verification process comes to being (see figure 2).
2. De manufacturer or parallel importer make sure that the prescription-only medicines in Europe are provided with a unique identification code (through a data matrix (2D) and in text) and an anti-tampering device, and that the product information and unique identifiers in the National systems are loaded.

Figure 2 – Verification process

- Manufacturers and parallel importers report all data from unique identification marks to the European hub (EMVS). Moreover, information on the packing status and organisation is delivered.
- The EMVS sends this data to the national hub (NMVS) where the packaging is offered to the market.
- Before dispense at the pharmacist registration of the medicine in the NMVS is verified.
- Wholesalers and parallel distributors carry out checks at products they ship, on the basis of standardised risk-analysis.



4. FMD and the financial implications for the manufacturers of generic medicines

4.2 Which additional costs for the Dutch manufacturers of generic medicine are brought along with the FMD?

Based on the data collected from the research, the average additional costs from the FMD in the Dutch market are estimated at € 0,17 per packaging per year. This concerns the average for the first 5 years after implementation of the FMD, where both initial costs made till 2019 and structural additional costs are carried along. Increases in wages and prices compared to 2017 are not taken into consideration.

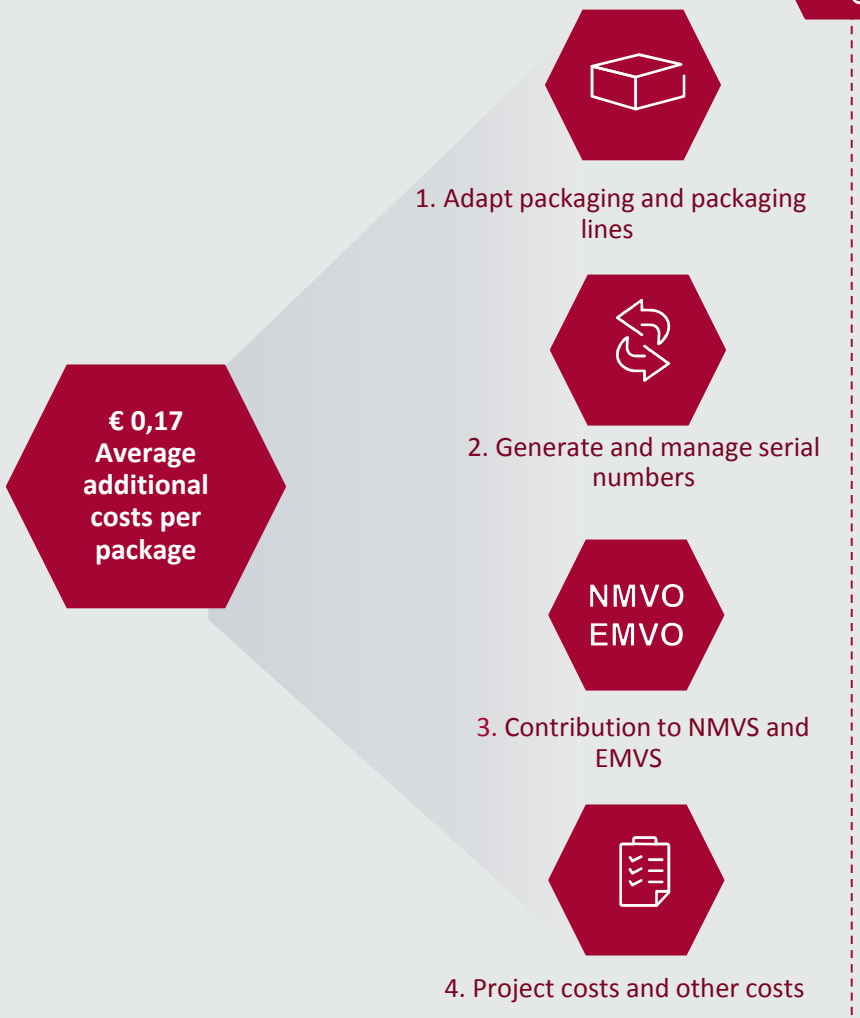
At determining the costs, we distinguished the following categories (see figure 3):

1. Adapt packaging and packaging lines
2. Generate and manage serial numbers
3. Contribution to NMVS and EMVS
4. Project costs and other costs (accidental)

The costs for packages and packaging lines (category 1) are passed on to the manufacturer/MAH by the producer or by a so-called contract packer. The production of medicines is often centralised for multiple countries by the manufacturer itself or a contractor. The medicines are traded through the MAH's in different countries. Also the packers work increasingly internationally. The costs mentioned under 2 till 4 are made by the manufacturer for the Dutch market.

The different cost categories will be discussed in the following sections.

Figure 3 – Additional costs FMD



4. FMD and the financial implications for the manufacturers of generic medicines

4.2.1 What are the additional costs for adapt the packaging and packaging lines

To determine the costs for adapting the packages and packaging lines, data from two Dutch packers were collected. Moreover, three manufacturers delivered additional information through their production sites and contract manufacturers. In total, this concerns the cost data of 30 packaging lines with roughly 45 million packages per year.

The packages lines are expanded with units with devices to apply the data matrix and the anti-tampering device. The adaptation of the packaging lines will take place gradually in the period of 2017-2019, so that from 9 February 2019 onwards, it is possible to comply with the FMD requirements.

On average, the adaptation of the lines will take 4 to 5 weeks; these costs for installation and testing are taken into account. Next to that, non-recurring costs are connected to the adaptation of packages (artwork), the software to apply the unique number which is exchanged with the contractor/MAH, the training of production staff and project costs. These costs, that occur prior to the implementation of the FMD, are considered on the basis of usual economic life including interest.

Structurally, costs are related to licenced software, materials and interest. Moreover, the FMD requires additional costs related to quality and data management. It is expected that as a consequence of adding a data matrix and anti-tampering device, there will be time delays in the lines, and more production losses will occur as a result of lost packages.

To calculate the costs per packages, the volume of packages produced annually by these packaging lines is taken as a starting point. A detailed explanation is given in Annex C.1; in section we also describe how the cost estimation has been established and to what extent the costs are substantiated.

Figure 4 - 1. Additional costs of packaging and packaging lines

Packaging/ packaging lines

Annual additional costs

One-off costs/investments:
a. Packaging lines
b. Set up and test
c. Artwork
d. (Implementation) software and dataconnections
e. Training
f. Project costs

Recurring costs:
g. Interest
h. Licences software
i. Materials
j. Quality management
k. Data management
l. Line speed reductie
m. Production loss

4. FMD and the cost consequences for the manufacturers of generic medicines

4.2.2 What are the additional costs for generating, exchange and management of serial numbers (serialisation)

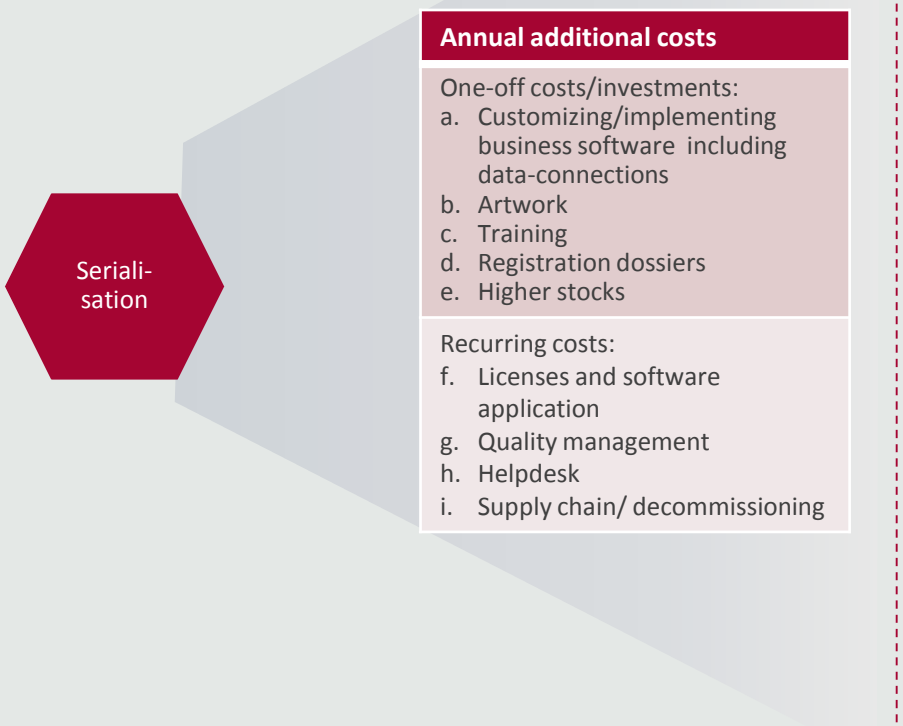
To determine these additional costs, we collected data from two manufacturers and their MAHs.

Manufacturers/MAHs make one-off costs related to customizing and implementing business software including data connections with the hubs, artwork, adjustments of registration dossiers and employee training. Also temporarily higher stocks are needed, thereby ensuring that the set-up and testing of packaging lines is captured and there is sufficient stock of registered medicines to catch any delay in delivery of packaging with serial numbers on February 9, 2019.

Structurally, costs arise due to licenses and software application management. Quality management requires a greater effort; serial numbers are added to the registration dossiers and it is necessary to ensure that the numbers are adequately exchanged with the EMVS/NMVS. There are also additional costs in the supply chain; drugs withdrawn from the market should be reported to the EMVS (decommissioning). Based on an estimate of the annual medicines withdrawn from the Dutch market by manufacturers, the operating costs are estimated.

The costs for serialisation are estimated per manufacturer/MHA and then calculated for the Dutch market, based on the number of packages. For a detailed explanation of the various costs and the calculation, see Appendix C.2.

Figure 5 – 2. Additional costs of serialisation



4. FMD and the cost consequences for the manufacturers of generic medicines

4.2.3 What are the additional costs for the NMVO en EMVO?

The EMVO is founded in 2015 by the European innovative industry (EFPIA), generic industry (Medicines for Europe), wholesale (GIRP), farmacists (PGEU) and parallel traders (EAEPC) to establish a safe, interoperable and cost-effective verification system across Europe.

The Dutch Medicines Verifciation Organisation (NMVO) builds, tests and fills the national database and carries out the connectivity process of all stakeholders and informs them about it.

The costs of the NMVO are reversed by all manufacturers and their MAHs who sell prescription drugs on the Dutch market. The cost consists of two parts:

- An entrance fee to cover the start-up costs;
- An annual contribution from January 2019 to pay the system's costs.

The entrance fee for the NMVO applies to each manufacturer/MAH in the Dutch market; this includes the start-up costs, which mainly include ICT and project costs. The recurring costs relate to the annual contribution for the ICT, helpdesk and governance.

It has been agreed that the start-up costs including the construction of the EMVS will be pre-financed by the EMVS initiators. Later these costs including interest will be passed on to the NMVOs. In addition, for all MAHs, an onboarding fee for the EMVO applies.

The entry fee and the structural costs of the NMVO (including EMVO costs) are attributed to the generic market on the basis of the number of MAHs (see also Appendix C.3).

Figure 6 – 3. Additional costs of NMVS en EMVS

NMVO EMVO

Develop-ment and manage-ment of data banks

Annual addtional costs
One-off costs: • Entrance fee NMVO • On boarding fee EMVO
Recurring costs: • Contribution to the NMVO

4. FMD and the cost consequences for the manufacturers of generic medicines

4.2.4 What are the project costs and unforeseen expenses?

Project costs

All manufacturers/MAH's make project costs for the introduction of the FMD. These start-up costs are written off in the calculation of additional costs in 5 years.

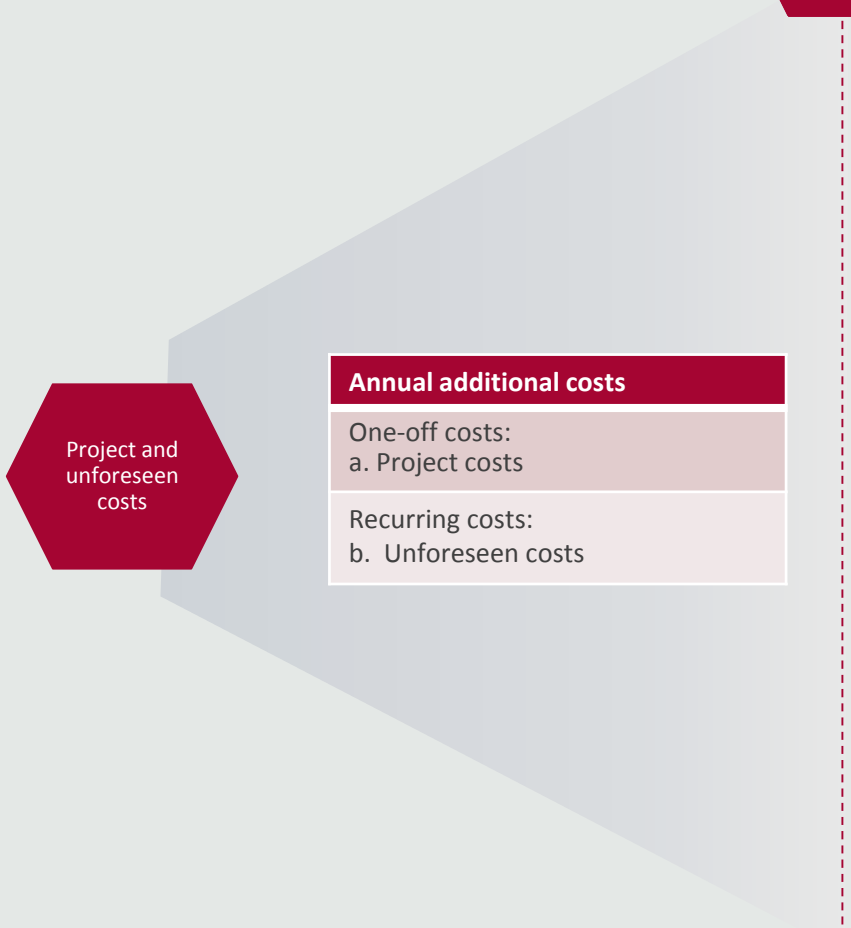
Accidental costs

There may be a number of unforeseen expenses due to the introduction of the FMD. The following have been put forward by manufacturers and packers:

- Unexpected expansion of packaging lines: The cost estimate assumes that the adaptation of current packaging lines is sufficient. The delay in production lines may also require expansion of packaging lines.
- Increase in lead times because packaging lines have not been adjusted in a timely manner or to a sufficient extent; this can affect sales.
- Registration costs in other countries: in the Netherlands there are no costs associated with adjusting registration dossiers. For medicines that enter the Dutch market by registration in other countries, such a fee can apply.
- Accidents with regard to, for example, transport, can imply that medicines can not be registered in the Netherlands on time before 9 February 2019.
- Problems with reading the data matrix or automated processing of packages. First tests show that adjustments are sometimes needed.

The unforeseen costs are estimated at 5% of the total additional costs of the FMD.

Figure 7 – 4. Project- en unforseen expenses



4. FMD and the cost consequences for the manufacturers of generic medicines

4.3 Wat affects the additional costs?

The costs presented in the previous section relate to an average per packaging. In this section we will examine which bandwidth can occur. We make a distinction between:

A. Costs of packaging and packaging lines (1)

For these costs, the volume per drug/product is important: Larger batches have on average a lower price. Figure 8 shows that the volume of products on the Dutch market is small: 50% of the packaging (more than 3,000 products) has a volume of less than 250,000 a year (see Figure 8).

B. Other costs (2, 3 and 4):

2. Generating/registering of serial numbers
3. Contribution to NMVS and EMVS
4. Project and other costs

These costs are made by manufacturer/MAHs and are largely fixed. The higher volume a manufacturer puts into the market, the lower the cost per packaging.

The generic market in the Netherlands is characterised by a relatively limited number of manufacturers; the top 10 almost determines the total volume (see Figure 9). In the top 10 there are also big differences in volume and therefore also in the additional costs per packaging.

Fig. 8 - Volume per medicinal product; 2016

- There is a limited number of products with a very large volume;
- There are many products with a very small volume (<250.000 per year)

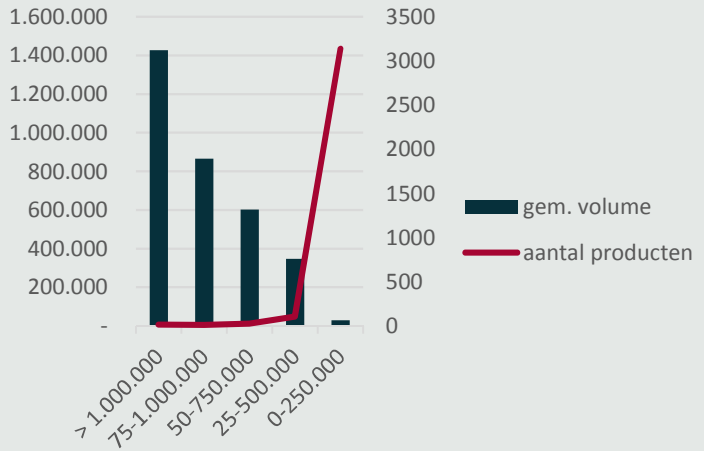


Fig. 9 - Volume per manifacturer (2016)

- There is a limited number of manufacturers with a very large volume;
- There are many manufacturers with a small volume

Manufacturers	Aandeel in volume
Top 10	97,3%
Top 20	99,6%

4. FMD and the cost consequences for the manufacturers of generic medicines

4.3 What is the bandwith of the additonal costs of the FMD?

4.3.1 Per manafacturer

The additional cost per packaging may vary considerably per manufacturer, because of the share of (semi) fixed costs associated with the introduction of the FMD. We calculated a bandwidth between € 0.12 and more than € 1.77 based on the number of packaging per year per manufacturer. In this calculation, the costs of packaging are calculated based on the composition of the assortment with a weighting of the size of the different products. The other costs are calculated based on the total volume.

We ignored small players in the Dutch market (with a total volume of less than 100,000 units). For these players, it is expected that the cost per packaging for the Dutch market will even be higher.

4.3.2 Per product category

The bandwidth can also be expressed by product category based on volume and associated selling prices. Indeed, medicines with a small volume usually have higher average prices and costs than medicines with a high volume. This variant is presented in Figure 11 based on volume and AIP prices.

A compensation based on such a method can work out differently per manufacturer - our analysis shows - because manufacturers have great differences in the composition of their assortment and the corresponding prices. Also, such a compensation for manufacturers with a small assortment (not belonging to the top 10) on the Dutch market will generally not be sufficient given the bandwidth presented in section 4.3.

Fig. 11 – Allocation per product category; a variant; 2016

Category	Allocation of costs
less than 100.000	0,34
100-250.000	0,12
250.000 - 1.500.000	0,09
more than 1.500.000	0,06
total	0,17

Calculation per producategorie by volume off packaging and AIP-prices (AIP-revenues) 2016

4. FMD and the cost consequences for the manufacturers of generic medicines

4.4 What are the social benefits of the FMD?

The FMD aims to achieve greater patient safety. The legal supply chain is enhanced by this directive. This prevents counterfeits through the illegal circuit.

For the Netherlands, this effect of the FMD at this stage is expected to be limited as a result of the closed chain; only prescription medicines, with the many quality requirements under supervision of various authorities, are reimbursed under the Dutch Health Insurance Act.

There are more opportunities to realise social benefits through serialisation. Through the provision of a track and trace system throughout the supply chain, production and distribution could be further optimized and thereby reducing costs. Unlike the regulations in the United States for example, the FMD and the manner in which the NMVS is arranged does not provide such a system. The NMVS is only accessible for the various chain partners for verification and decommissioning of withdrawn medicines.

The data matrix on the packaging could provide patients with easier access to relevant information about the medicines which they have received (for example, indicating not likely combinations, timely re-ordering, access to package leaflet). Also in this regards, according to the FMD, the NMVS does not provide patients access to additional information about the drugs via the data matrix.

4.5 What are the benefits for the manufacturers?

Manufacturers of generic drugs in the Netherlands indicate that they do not distinguish benefits of the FMD for their own processes; benefits in the supply chain are missing (see section 4.4).

They do not expect a better market position due to the counterfeit medicines. For prescription drugs, as previously indicated, there is in the Netherlands a closed system of delivery and compensation that (largely) prevents fraud.

4. FMD and the cost consequences for the manufacturers of generic medicines

4.5 What costs were estimated for manufacturers by the EU?

The European Commission carried out an impact analysis in 2015 to determine the effect of FMD on the price of drugs. Costs per packaging were estimated by the European Commission to be up to 3 eurocents per packaging (see Figure 11). In this study, no distinction was made between generic drug manufacturers and innovative medicines. The European Commission's research is based on parameters that are not explained, therefore, we are unable to create a detailed comparison.

Medicines for Europe (the Association of European generic manufacturers) has expressed concerns about the research results and has pleaded for a weighted impact assessment that distinguishes between costs for generic drugs and innovative manufacturers.

Based on our research, we get a significantly higher average price than published by the European Commission. It is important to note that we have only investigated the costs of generic drug manufacturers. Next to that, we reasoned from the Dutch market and the associated cost structure and market volumes.

Figure 11: Difference in cost estimation per packaging

- Generic and innovative medicines
- European market

ECORYS

- Generic medicines
- Dutch market

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* Source: European Commission, FMD Impact Assessment (2015)

5. Impact of the FMD on the Dutch generic market

5.1 The generic market in the Netherlands

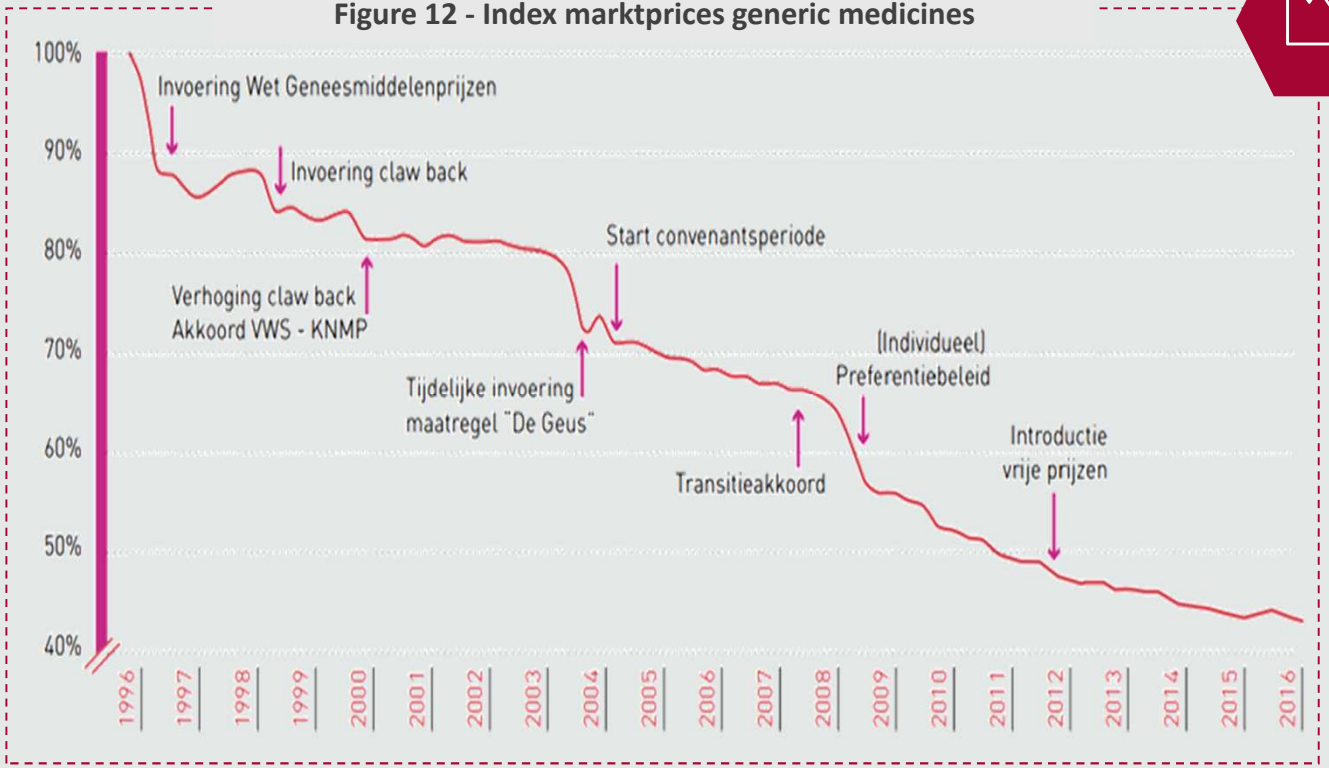
The market for generic drugs in the Netherlands has increased significantly over the last decade. In 2005, Dutch pharmacists provided generic medicines in 51.8% of the cases; in 2016 this was 74.1%. With this percentage, the Netherlands is in the top of Europe. In 97.1% of the cases, pharmacists supply a generic medicine when such a variant is available (source SFK, 2016). The average price of a generic drug per 30 tablets is only 2.60 euros. This way, generic drug manufacturers make an important contribution to the affordable supply of medicines in the Netherlands.

In recent years there has been an increasing pressure on the prices of generic medicines (see Figure 12). The preferential policies of health insurers, introduced in 2009, and the introduction of "free" prices in the context of the Dutch law on medicine prices (Wet Geneesmiddelenprijzen (WGP)) in 2012 have resulted in price pressure and heavy price competition.

For patients, health insurers and the government, low medicine prices are favorable while this causes problems for generic drug manufacturers. The fall in market prices has sharpened the margins.

Dutch manufacturers of generic medicines have only limited margins (EBITDA was only around 6% in 2016). Because the margins are already so small, new regulations from the EU or at national level have an important impact.

Figure 12 - Index marktprices generic medicines



Source: Stichting Farmaceutische Kengetallen (2016; 2017) Bogin (2017)

5. Impact of the FMD on the Dutch market of generic medicines

5.2 What are the consequences of the prices of generic medicines?

In chapter 4 we estimated the mean additional costs of the FMD at € 0,17 per packaging with a rather big bandwith per manufacturer. In addition, we assume that the costs, including initial costs incurring during the period to 2019, will be repaid in 5 years. Part of these additional costs remain structurally after those 5 years (expected to be around 75% of the total additional costs).

The average additional cost of FMD is significant in relation to the average AIP price of generic drugs (2.60 euro per 30 tablets).

The additional costs of manufacturers to meet the FMD would normally be credited to market prices. However, practice appears to be more complex. The Medicines Prices Act (WGP) sets price limits based on historical international comparisons. In addition, manufacturers have to deal with the preferential policies of health insurers, which makes it difficult to pass through the additional costs.

5. Impact of the FMD on the Dutch market of generic medicines

5.3 What are the consequences for the availability of medicines?

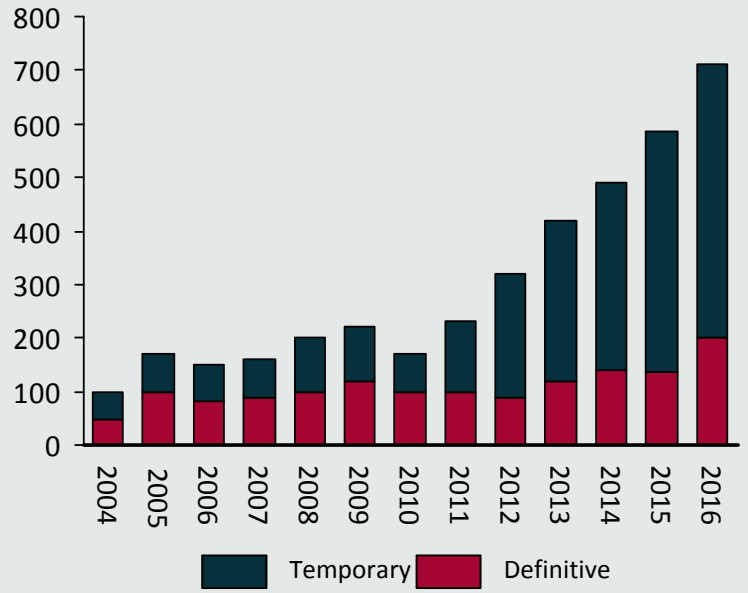
Small margins force manufacturers to work more cost-efficiently. One solution for manufacturers or wholesalers is to keep less expensive supplies. However, this would mean that production and delivery problems, wherever they occur, have a greater impact on the availability of drugs.

For medicines that are not available for more than 14 days, pharmacists notify the KNMP. By 2016 there were 710 reports of a drug shortage by pharmacists; this means the number of drug shortages in the Netherlands is further increasing (see figure 13). The non-availability of drugs has negative effects on the patient and involves significant costs. Therefore, pharmacy parties and the Ministry of Health recently agreed to improve the reporting system and make timely actions to improve the availability of drugs.

It can be expected that the FMD has a negative effect on availability. Firstly, before February 2019 all packaging lines will have to be adjusted. This causes a production stop of about 4-5 weeks per packaging line. The production of medicines and packaging cannot be easily transferred because of the necessary permissions. Additionally, the FMD adds complexity, especially in the start-up phase, affecting the speed of production lines and the production process.

Second, when the additional costs cannot be passed on (directly), the FMD will cause further deterioration of the margin. This will lead manufacturers to aim for even more efficiency and less stock. In addition, manufacturers can choose not to market certain products anymore (see also Figure 13). It is expected that this will apply especially to manufacturers with small volumes and low prices in any market. There are already signals of manufacturers taking their products of the (Dutch) market as a result of the FMD. The start-up costs and investments are too high in relation to the revenues.

Figure 13 – Shortages of medicines*



*Generic and innovative medicines

Source: KNMP (2017)

6. Conclusion

Compared to other countries, the Netherlands has a large proportion of extramural generic drugs (74%) with relatively low prices (17% of total costs). With that, generic drug manufacturers make an important contribution to the affordable supply of medicines in the Netherlands.

The FMD involves substantial costs for generic drug manufacturers in the Netherlands. These additional costs amount to an average of € 0.17 per packaging, 6.5% of the average price (AIP) per box of 30 tablets. The total additional costs are estimated at a volume of more than 180 million (including delivery to hospitals and other institutions) of approximately 30 million euro per year. The additional costs for a great deal are caused by the adjustment of packaging lines. In addition, there are significant additional costs associated with generating and reporting the unique serial number to the European and national databases and participation in these costs.

The costs of the FMD vary by manufacturer depending on the total production volume and range. Especially for manufacturers with relatively small volumes on the Dutch market, the costs are high. An important part of the costs of the FMD are linked to substantial investments without the guarantee that these costs will be reimbursed. The FMD can thus have a disproportionate effect on different manufacturers or the products they provide, causing shifting competitive positions.

It may be expected that FMD will also have an effect on the availability of medicines on the Dutch market. In addition, from the date the FMD enters into force, the delivery of drugs may come under pressure when the packaging lines in the Netherlands and elsewhere fail to be operational in time.

The margins of generic drug manufacturers in the Netherlands are low. Therefore, the mentioned effects can be expected to occur to a greater extent when generic drug manufacturers are not (in a timely manner) able to pass on the costs associated with the FMD. The regulations in the Netherlands interfere with price adjustments due to the FMD; the regulation of prices of prescription medicines (WGP) takes into account historical prices. The additional costs of the FMD will not be processed at the start in 2019. This can have important consequences for the compensation of cost for patients (under the reimbursement system GVS). The WGP will be revised in the coming years. The effects of the FMD, by comparing prices with other countries which have a different market structure, cannot yet be estimated properly.

This confirms that Bogin sets high store by reaching solutions with VWS and health insurers to pass on the costs of the FMD. In addition, a “compensation strategy" should be developed that can be realised in the short term and can make the difference in costs that occur for the different manufacturers.

Appendices:

A. Guidance committee

B. Consulted documents

C. Explanation estimated additional costs

Appendix A: Guidance committee

Bob Beekman	Teva
Martin Favié	Bogin
Dirk Groen	Mylan
Hennie Henrichs	Teva
Emile Loof	Disphar
Erwin van Malland	NMVO
Pieter Vercruysse	Tjoapack
Armand Voorschuur	Dutch Association of Innovative Medicines
José Puiman	Ministry of Health (listener)
Martin Potjens	ZN, Dutch Association of Health Insurers (tot 1/10/2017)
Ulco Visser	Apotex

Capgemini Consulting:
Lex van der Ham
Sarah Prins
Willem Sträter

Capgemini Consulting

Appendix B. Consulted documents

- Website Bogin (2017)
  http://www.bogin.nl/
- Damadoran database, Cost of capital by industry sector (2017)
  http://pages.stern.nyu.edu/~adamodar/New_Home_Page/datafile/wacc.htm
- European Commission, Impact Assessment supplementing Directive 2001/83/EC of the European Parliament and of the Council (2015) http://ec.europa.eu/smart-regulation/impact/ia_carried_out/docs/ia_2015/swd_2015_0189_en.pdf
- European Medicines Agency, Falsified Medicines (2017)
  http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000186.jsp
- GS1, FMD directive - Impactanalyse voor de Nederlandse geneesmiddelenketen (2017)
  https://www.gs1.nl/sites/default/files/gzhz_fmd_impactanalyse.pdf
- KNMP, Voorstel lage prijzen en een beter beschikbaarheid van geneesmiddelen (2017)
  https://www.knmp.nl/downloads/knmp-voorstel-lage-prijzen-en-een-betere-beschikbaarheid-van-geneesmiddelen.pdf
- Medicines for Europe, Advice on the implementation of the EU-Directive (2013)
  http://www.medicinesforeurope.com/wp-content/uploads/2016/03/Advice_on_the_implementation_of_EU-Directive_201162EU_FINAL_WEB.pdf
- Stichting Farmaceutische Kengetallen, Data en Feiten (2016)
  https://www.sfk.nl/publicaties/data-en-feiten/data-en-feiten-2016
- Stichting Farmaceutische Kengetallen, Data en Feiten (2017)
  https://www.sfk.nl/publicaties/data-en-feiten/data-en-feiten-2017

Appendix C: Explanation estimated additional costs

1. Adopt packaging and packaging lines: a and b

a. Investments

- *Explanation:*

  Adoption of the packaging lines is necessary to provide a data matrix and anti-tampering device; as a rule, an additional unit is added.

- *Available information:*

  The costs of these units are largely known; the first investments in packaging lines have been made. We received a calculation of two packers and two manufacturers who take care of some of the packaging themselves. The volume per packaging line is different, which explains the big variations in the additional cost per packaging. The differences in volume are caused by the volume per batch and the packaging type. The costs of adjusting the boxes, the most common package form, in our sample are the lowest; Other packages like bags and pots (in total 3% of the volume included in our calculation) know a higher cost price (about 2x the price of a box). For bandwidth, we have made an approximation based on the batch size per packaging line.

- *Estimation:*

  We use a 5-year depreciation period for the calculation of the cost of these investments. The annual depreciation costs of 26 packaging lines are divided by the production of packaging for these lines.

- *Foundation:* 
  - Very similar investments per packaging line/unit between manufacturers and packers;
  - The sample includes almost 30% of the total volume of packaging delivered in the Netherlands;
  - Differences between type of packaging has been included in the estimation of investments.

b. Setup and testing

- *Explanation:*

  For the set up and testig of the new units of the packaging lines are closed for 4-5 weeks.

- *Available information:*

  This 4-5 week standstill is based on experience with customizing first packaging lines with one producer and one packer

- *Estimation:*

  We use a depreciation period of 5 years for the calculation of the cost of this standstill.

  To calculate the costs of shutting down the packaging lines for 4-5 weeks we used the lost margin. The 'margin loss' is divided by the production of packaging for these lines. This calculation method assumes that there are no additional production losses.

- *Foundation:* 
  - Calculation is based on assumptions of average margins;
  - These are approached based on data from the annual accounts;
  - Chosen method for standstill is based on sales loss ,this is an approach.

Appendix C: Explanation estimated additional costs

1. Adapt packaging and packaging lines: c, d and h

c. Adjustment artwork

- *Explanation:*

  For all products, the artwork must be fully customized to meet the FMD.

- *Available information:*

  The costs are specified by a manufacturer and a packer. They have made an estimate of necessary adjustments. The costs depend on the number of products. Our estimation is based on the number of products that were applicable in the Netherlands in 2016.

- *Calculation:*

  We apply a 3-year depreciation period for these costs. The costs of the manufacturer and packer are the basis.

- *Foundation:* 
  - Estimation of manufacturer and packer based on previous artwork adjustments;
  - Accurate cost estimation based on hours (FTE).

d. and h. Software

- *Explanation:*

  The software for the packaging lines needs to be adjusted. These are related to implementation and licensing costs. Additionally, a data exchange with suppliers must also be established.

- *Available information:*

  The stated costs of the manufacturer and packer are the basis.

- *Calculation:*

  We apply a depreciation period of 5 years for the implementation cost. Licensing cost are annual. The cost per packaging is calculated on the basis of the number of packages estimated by the packer per year.

- *Foundation:* 
  - The estimate was made based on information from software vendors;
  - Generally, the costs of software are known.

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Appendix C: Explanation estimated additional costs

1. Adapt packaging and packaging lines : e and f

e. Training

- *Explanation:*

  The cost incurred to instruct production staff about the changes in the packaging process.

- *Available information:*

  A manufacturer and packer accounted for their costs for training. An estimation was made based on other projects.

- *Calculation:*

  We have taken the estimated training costs for the manufacturer and packer based on a 3-year depreciation divided by the estimated number of packages.

- *Foundation:* 
  - Estimation of manufacturer and packer based on experiences;
  - The stated costs are very similar.

f. Project costs

- *Explanation:*

  The project costs come from implementing the changes required by the FMD and the possibility of hiring external advisors.

- *Available information:*

  We take into account the costs given by a manufacturer and packer. An assumption of the project cost are based upon previous projects and the impact of changes required by the FMD.

- *Calculation:*

  The projected costs for the manufacturer and packer are used as a starting point. We use a depreciation period of 3 years and the cost per packaging is calculated based on the estimated number of packages produced (by the packer per year).

- *Foundation:* 
  - Estimation of manufacturer and packer based on experiences;
  - The stated costs are very similar.

Appendix C: Explanation estimated additional costs

1. Adapt packaging and packaging lines: g and i

g. Interest

- *Explanation:*

  A market-based interest rate of 7.76% is calculated for loans for the adaptation of packaging lines.

- *Available information:*

  We take the investment given by a manufacturer and packer as a starting point

- *Calculation:*

  Interest based on a straight line depreciation.

- *Foundation:* 
  - Investments are known as well as the market-based interest rates.

i. Materials

- *Explanation:*

  This applies to additional materials (ink and seals).

- *Available information:*

  We take in account the costs specified by a manufacturer and packer based on estimations and historical costs.

- *Calculation:*

  We have taken the estimated project costs for the manufacturer and packer per year, divided by the estimated number of packages.

- *Foundation:* 
  - Estimation of manufacturer and packer based on experience and historical costs.
  - The stated costs are very similar.

Appendix C: Explanation estimated additional costs

1 Adapt packaging and packaging lines: j and k

j. Quality management

- *Explanation:*

  The adjusted packaging lines ask for a new way of administration. This has to be managed and controlled.

- *Available information:*

  We take the cost specified by a manufacturer and packer. An estimate has been made of the additional necessary FTE for quality management.

- *Calculation:*

  We have taken the estimated annual cost of the manufacturer and packer as a basis, divided by the estimated number of packages.

- *Foundation:* 
  - Estimation of manufacturer and packer based on experience data
  - Accurate cost estimation based on hours (FTE).

k. Data management

- *Explanation:*

  Generating and managing identification codes puts extra pressure on existing and new data processes.

- *Available information:*

  We took in account the data management costs specified by a packer. The packer has made an estimate of the additional necessary FTE and related cost.

- *Calculation:*

  We have taken the annual estimated additional costs for the manufacturer and packer as a basis, divided by the number of estimated packages.

- *Foundation*: 
  - Estimation of packer based on earlier data management projects.

Appendix C: Explanation estimated additional costs

1. Adapt packaging and packaging lines: l and m

l. Delay of packaging lines

- *Explanation:*

  By adjusting the data matrix and adding the anti-messing system, a delay on the packing lines will occur.

- *Available information:*

  Experiences in other countries show that in the first year the delay is 30%; in the next few years this percentage will fall to 10% and possibly lower. Based on these experiences, we estimate an average of 10%.

- *Calculation:*

  We provide an additional 10% required capacity (packaging lines and staff) based on the specified cost of one packer.

- *Foundation:* 
  - The cost estimate is based on experience data from packers in other countries.

m. Production loss

- *Explanation:*

  Applying the data matrix on the packaging and adding the anti-tampering device significantly increases the complexity of the production process. This increases the probability of loss of production due to failures.

- *Available information:*

  We take in account the costs specified by a manufacturer and a packer. An assessment has been made by them of the additional necessary controls and related human resources.

- *Calculation:*

  The cost for the additional necessary controls estimated by the manufacturer and packer are divided by the estimated number of packages.

- *Foundation:* 
  - Estimate of the manufacturer and the packer based on experiences.

Appendix C: Explanation estimated additional costs

2. Generating and managing serial numbers: a, f and b

a. en f. Customization of business software including data-connections

- *Explanation:*

  The business software must be adapted and implemented. Important costs are associated with data connections with EMVS/NMVS and manufacturers/packers.

- *Available information:*

  The data are provided by two manufacturers/ MAHs and based on inventory of their ICT suppliers.

- *Calculation:*

  Customization software and implementation costs are written of in 3 years.

- *Foundation:* 
  - The estimate was made on the basis of information from software vendors;
  - Generally, the cost of software is known.

b. Artwork

- *Explanation:*

  The artwork has to be designed and the specifications must be communicated with the production sites and / or packaging.

- *Available information:*

  We take the cost specified by a manufacturer and packer in account. An estimate of these costs has been made by them based on experience.

- *Calculation:*

  The costs for the additional necessary controls estimated by the manufacturer and packer are divided by the estimated number of packages.

- *Foundation:* 
  - Estimate of manufacturer and packer based on earlier artwork adjustments;
  - Accurate cost estimate based on hours (FTE).

Appendix C: Explanation estimated additional costs

2. Generating and managing serial numbers: c and d

c. Training

- *Explanation:*

  In preparation for the introduction of the FMD, additional training is required.

- *Available information:*

  The data are based on information supplied by a manufacturer/MAH. The data–are very similar and further substantiated in hours and numbers.

- *Calculation:*

  The costs of training are calculated by the volume of packages and depreciated in three years.

- *Foundation:* 
  - Estimate of manufacturer by experiences.
  - Accurate cost estimate by hours (FTE)

d. Registration dossiers

- *Explanation:*

  The registration dossiers should be updated and registered with CBG or elsewhere.

- *Available information:*

  We accept the manufacturer's stated cost. An estimate has been made of these costs per product based on experiences; the stated costs of both organisations are very similar.

- *Calculation:*

  Cost of the necessary additional controls divided by the estimated number of packages.

- *Foundation:* 
  - Estimates by manufacturers based on experience data;
  - Accurate cost estimation by hours (FTE).

Appendix C: Explanation estimated additional costs

2. Generating and managing serial numbers: e and g

e. Higher stocks

- *Explanation:*

  In preparation for the introduction of the FMD, additional stocks will be required. Manufacturers have the obligation to deliver-while there are limitations in capacity. The cost of stocks is high and will be formed with policy. The size is carefully estimated at about 1 month.

- *Available information:*

  A manufacturer deliverd the data.

- *Calculation:*

  The stocks are calculated based on the volume (one month, the cost of inventory) and depreciated over three years.

- *Foundation:* 
  - The cost estimate is based on the assumption of additional stocks of one month (estimate).

d. Quality management

- *Explanation:*

  The cost of quality management is higher due to the additional requirements in the context of serialization (supplying data to EMVS / following decommissioning, etc.).

- *Available information:*

  We accept the manufacturer's stated cost. An estimate has been made of the required FTE.

- *Calculation:*

  The costs of extra FTE are divided by the estimated number of packages.

- *Foundation:* 
  - Estimate based on the manufacturer’s experience.

Appendix C: Explanation estimated additional costs

2. Generating and managing serial numbers: h and i

h. Helpdesk

- *Explanation:*
  In preparation for the introduction of the FMD, additional questions will be directed towards the helpdesk

- *Available information:*
  The data are based on estimates of the number of FTEs provided by a manufacturer/MAH.

- *Calculation:*
  The costs of these FTE's are taken in account and divided by the number of packages.

- *Foundation:* 
  - Accurate cost estimated per hour(s) (FTE).

i. Supply chain / decommissioning

- *Explanation:*
  Additional costs in the supply chain especially by decommissioning.

- *Available information:*
  An estimate has been made of these costs based on FTEs and the number of packages for which decommissioning is necessary (scanning / unpacking).

- *Calclulation:*
  The supply chain / decommissioning costs are divided by the estimated number of packages.

- *Foundation:* 
  - Estimate of manufacturer's supply chain costs by experience;
  - Accurate cost estimate by number of yearly number of packages to be decommissioned.

Appendix C: Explanation estimated additional costs

3. EMVO and NMVO

- *Explanation:*

  The Stichting Nederlandse Medicijnen Verificatie Organisatie (NMVO) guides the creation of the NMVS in the Netherlands. It builds, tests and fills the national database, takes care of the data connection process of all concerned and informs them about it. The EMVS will charge the start-up and other costs to the various NMVOs. Also, for all MAHs a one-time onboarding fee applies.

- *Available information:*

  We take into account the costs specified by the NMVO. The start-up costs of EMCDDA and NMVO are estimated for the period up to 2019; This also applies to annual governance, ICT and help expenses.

- *Estimation:*

  The costs are attributed to the manufacturers of generic drugs based on the number of MAHs. The costs are then divided by the number of packages.

- *Foundation:* 
  - The various costs are well-founded on the basis of a budget. The ICT-and project costs are the largest items. These are based on contracts agreed with ICT suppliers.
  - The allocation of these costs is based on the number of MAHs of generic drugs.

Appendix C: Explanation estimated additional costs

4. Project costs en other costs (accidental)

Project costs:

- *Explanation:*
  Project cost are made to prepare and guide the implementation of the FMD.

- *Available information:*
  The estimated costs of two manufacturers are taken in account.

- *Calculation:*
  The project costs are divided by the number of packages.

- *Foundation:* 
  - The project costs are estimated based on an estimation of the required capacity to prepare and guide the implementation of the FMD.

Unforeseen costs:

- *Explanation:*
  There will be unforeseen costs, because of many changes in the operating procedures (see section 4.2.4).

- *Available information:*
  Experiences of other projects.

- *Calculation:*
  We took in account 5% of the total additional costs for the FMD.

- *Foundations:* 
  - Based on experiences of other projects.