Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

Summary Report for Importation of Unlicensed Medicines

01 Jan 2015 – 31 Mar 2015

Author	**G. P. Matthews**	Date: 01-Sep-2015
Approved	**S. Bax**	Date: 01-Sep-2015

Contents

1 Introduction and Summary

This report covers the period 01-January-2015 to 31-March-2015 and shows the import notification system to be operating substantially within the requirements of SI 2012/1916.

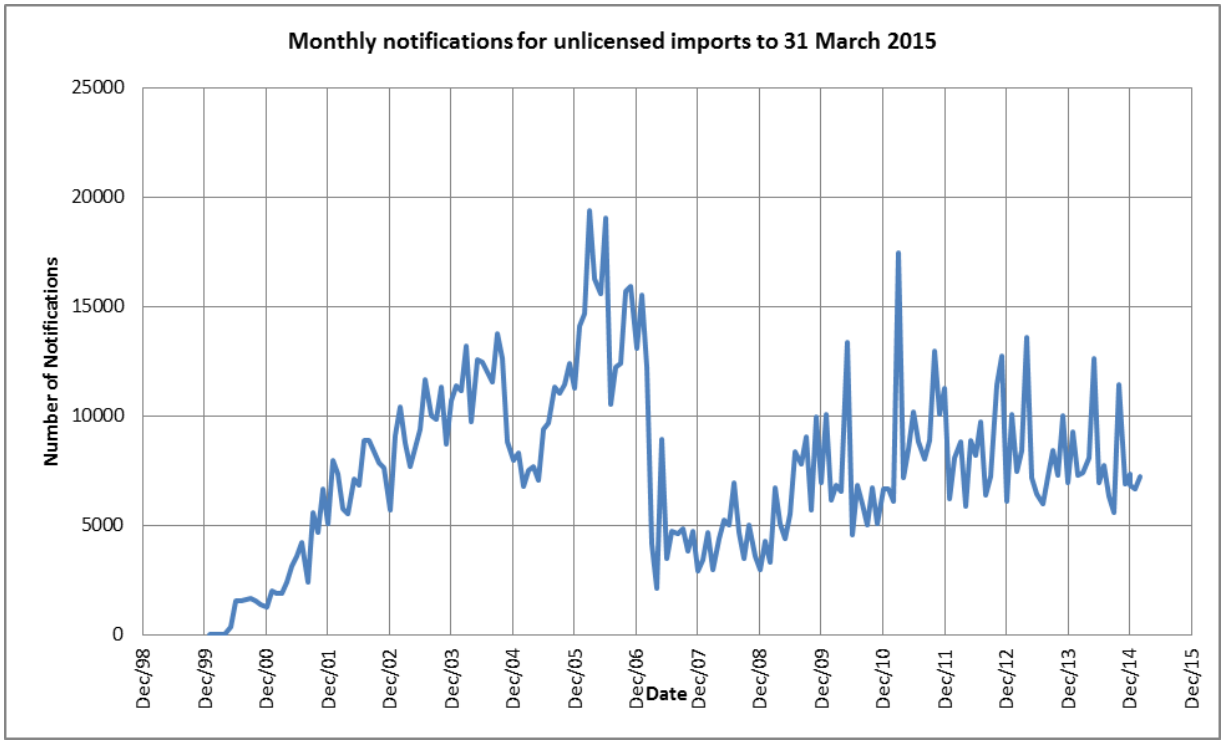
Objections to import continue to arise from notifications from prospective importers who do not possess the correct licence. A Wholesale Dealer's Authorisation, WDA(H) is required for importation of unlicensed medicines from elsewhere in the EEA and a Manufacturer's "Specials" Licence, MS, is required for importation from outside the EEA. In each case the licence must bear the correct category for these activities.

Objections to import have also been raised when importers have notified for importation where there is an equivalent licensed product available in the UK (or an equivalent product with a centrally issued Marketing Authorisation within the EEA). Importers must ensure they have robust procedures in place to check whether there is a licensed product available in the UK (or for centrally authorised products, within the EEA) that can meet the clinical needs of the patient(s). No special clinical need exists if there is an equivalent licensed product available, and notifications for import will attract objections unless there is a clinical reason why an apparently equivalent licensed product cannot be used. Importers should note that this also applies when a licensed equivalent product becomes available where previously no such product existed.

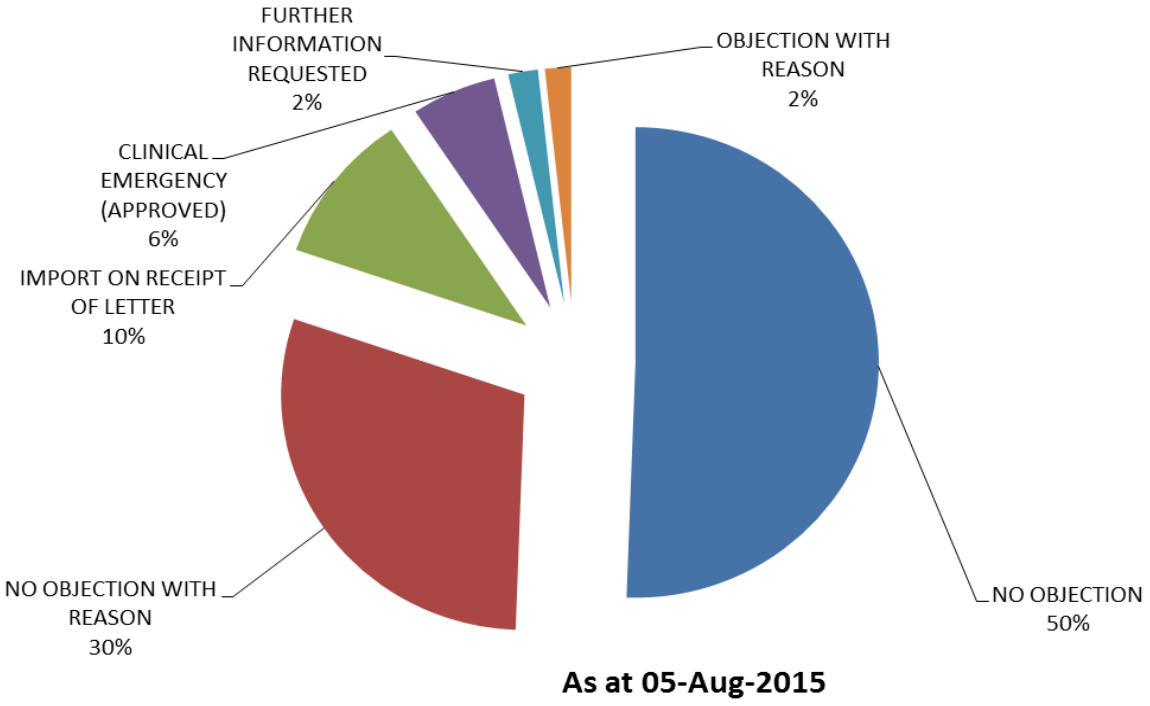
2 Notifications for importation

Graph 1 Monthly notifications for unlicensed imports

Note: Excludes invalid and cancelled notifications



Graph 2 Breakdown of valid notifications by status, 01 Jan – 31 Mar 2015



2.1 Importers

A total of 20677 notifications were received from 74 importers for the period 01 Jan 2015 to 31 Mar 2015. Of these, 6 importers accounted for approximately 75%.

Table 1 Valid notifications by importer 01 Jan 2015 to 31 Mar 2015

Importer Name	Number of Notifications	Percentage Share
74 Importers	**20677**	100%
Of which 6 importers	**15644**	~75%

2.2 Countries of export of products

Table 2 Countries of export 01 Jan 2015 to 31 Mar 2015

Rank	Exporting Country	Number of Notifications	% Share
1	United States of America	5275	25.51%
2	Germany	4342	21.00%
3	Italy	1651	7.98%
4	Spain	1250	6.05%
5	France	1111	5.37%
6	Canada	981	4.74%
7	Australia	827	4.00%
8	Czech Republic	760	3.68%
9	India	727	3.52%
10	Switzerland	638	3.09%
11	Slovakia	520	2.51%
12	The Netherlands	422	2.04%
13	Austria	391	1.89%
14	Belgium	338	1.63%
15	Denmark	315	1.52%
16	Republic of Ireland	268	1.30%
17	Sweden	218	1.05%
18	Portugal	126	0.61%
19	Poland	102	0.49%
20	Argentina	79	0.38%
21	Japan	79	0.38%
22	Norway	60	0.29%
23	Greece	50	0.24%
24	New Zealand	43	0.21%
25	Hungary	41	0.20%
26	Finland	32	0.15%
27	United Kingdom*	16	0.08%
28	China	12	0.06%
29	Puerto Rico	2	0.01%
30	Romania	1	0.00%
	Sum:	**20677**	**100.00%**
	EEA	**12014**	**58.10%**
	Non-EEA	**8663**	**41.90%**

*UK is not an acceptable country of import!

2.3 Most frequently notified products

Table 3 Top 50 frequently notified products 01 Jan 2015 to 31 Mar 2015

Rank	Product Name	Number of Notifications
1	Vitamins - Oral Preps	1242
2	Homoeopathics & Herbals	941
3	Melatonin Oral Preps	737
4	Cotrimoxazole Injections/Infusions	686
5	Thyroid Oral Preps	645
6	Gutron 2.5mg & 5 mg Tablets	640
7	Bisacodyl Enemas 10mg	554
8	Co-Proxamol Tablets 32.5/325mg	512
9	Povidone-Iodine 50 mg/ml Soln For Inj	440
10	Metolazone 2.5&5mg Tabs	422
11	Acetylcysteine Oral Preps	413
12	Fosfomycin Oral Preps	364
13	Progesterone Injections 100mg/1ml	313
14	Benzathine Benzylpenicillin Injections	265
15	Povidone-Iodine 10% Ointment	251
16	Measles + Rubella Vaccines	250
17	Monocomponent Measles Vaccines	250
18	Clindamycin 75MG/5ML Oral Suspensions	247
19	Allergy Tests	229
20	Tretinoin/Vitamin A & Hydroquinone Topicals (Creams Oints., Gels Etc.)	229
21	Sodium Nitroprusside 50mg Inj/Infn	229
22	Ticarcillin + Clavulanic Acid 3.1g Powder For IV Injection	212
23	Fumaric Acid Esters 30 &120mg Tablets	200
24	Sucralfate Oral Preps	186
25	Cyclosporin Ophthalmic Preps	183
26	Povidone-Iodine 5% Ophthalmic Solution	183
27	Melphalan 50 mg Injn/Infusn	175
28	Furosemide 20 mg/2 ml Solution For Injection	168
29	Ramucirumab 100 mg/10 ml - Conc For Solut for Infusion	160
30	Dasabuvir Tabs 250mg	154
31	Ombitasvir/Abt-450/Ritonavir Tabs	154
32	Tecemotide 279mcg Inj Suspn	152
33	Pridopidine (Acr16) 45 mg Capsules	150
34	Clonazepam 1mg/ml Injections	144
35	Idebenone Capsules & Tablets, All Strengths	144
36	Mexiletine CAPSULES All Strengths	142
37	Indigo Carmine Injections	141
38	Triamcinolone Acetonide/Hexacetonide Injections	138
39	Dhea Capsules All Strengths	134
40	Ornithine Aspartate Granules for Oral Sol 3&5g	131
41	Lu-DOTA, Tyr Ocfreotate, Lutetium-177 (^{177}Lu) Labelled	130
42	Flunarizine Capsules & Tablets All Strengths	126
43	Pirenzepine Tablets 50mg	121
44	Diazoxide Suspension 50mg/ml	119
45	Chlorothiazide Orals Preps (Tabs, Suspn)	111

Rank	Product Name	Number of Notifications
46	Potassium Chloride Controlled Release Tabs & Caps	110
47	Betamethasone 4mg/1ml Injections	108
48	BCG Injections, Instillations, Infusions	100
49	Demeclocycline Tablets & Caps, All Strengths	93
50	DTAP/IPV/HIB Vaccines	93

2.4 Vaccines and immunoglobulins

Table 4 Vaccines & immunoglobulins 01 Jan 2015 to 31 Mar 2015

Rank	Product Name	Number of Notifications
1	Measles + Rubella Vaccines	250
2	Measles Vaccines	250
3	BCG Instillations And Vaccines	100
4	DTAP,IPV,HIB Vaccines	93
5	DTAP Vaccines	30
6	Inactivated Polio Vaccines	30
7	DTAP,HEP B,IPV,HIB Vaccines	26
8	DTAP,IPV Vaccines	20
9	Tetanus Vaccines	20
10	Lymphocyte Immune Globulin Anti Thymocyte Globulin (Equine)	17
11	Measles + Mumps + Rubella + Varicella-Zoster Vaccine (Live Attenuated)	16
12	Diphtheria & Tetanus Combined Vaccine	10
13	Anti-Rho (D) Immune Globulin (Human)	3
14	Varicella Zoster Immunoglobulin	3
15	Antithymocyte Globulin - Equine	2
16	IgM Enriched Normal Human Immunoglobulin	2
17	Tetanus Immunoglobulin	2
18	Anti Human-T-Lymphocyte Immunoglobulin	1
19	CMV Immunoglobulin	1

2.5 Shortages

Table 5. Products notified claiming UK product shortages, 01 Jan 2015 to 31 Mar 2015

Product Name	Number of Notifications
Co-Trimoxazole Injections	739
Progesterone Injections 100mg/ml	271
Ticarcillin + Clavulanic Acid 3 g + 100mg Inj	206
Potassium Chloride Sr Tablets & Capsules	110
Betamethasone Sodium Phosphate 4mg/1ml Injection	100
Sucralfate Oral Preps	100
Demeclocycline 150 & 300 mg Oral Preps	93
DTAP/IPV/HIB 0.5ml PFS	92

Product Name	Number of Notifications
BCG Instillations & Vaccines	91
Digoxin 0.25mg/ml Injections	70
Iobitriodol Preparations	60
Liothyronine Hydrochloride Tablets 20 & 25 mcg	40
Co-Phenotrope 2.5mg And 25 mcg Tabs	22
Mitoxantrone Inj 20 mg/10 ml	21
Tetanus, Diphtheria, Pertussis And Polio Vaccines	20
Testosterone 100 mg Pellets	16
Vasopressin 20 Units/ml Inj Soln	15
Triamcinalone Acetonide 10mg/ml Inj Susp	12
Disulfiram 500 mg Tablets	8
Ketamine Injections	8
Lorazepam 2 mg/ml Injection Soln	8
Phentolamine Inj 10mg/ml	8
Acetazolamide Acetazolamide 250 mg Tablets	6
Aciclovir Eye Ointment 3%	5
Ascorbic Acid 500mg/5ml Inj	4
Tetracosactide Acetate Inj	4
Edrophonium 10mg/ml Injection	3
Perphenazine 2 & 4 mg Tabs	3
Chloramphenicol Sodium Succinate 1 g Powder For Inj	2
Prothionamide Tablets 250mg	2
Acetazolamide Inj 500mg	1
Acetylcysteine 200mg/ml Soln For Inj	1
Amino Acid Solution For Infusion	1
Factor Xi 1000 IU Inj	1
Isoniazid Powder For Infusion 500mg	1

NOTE: This listing is indicative only and not exhaustive. It is based upon text comments in the imports database.

3 Administrative matters

3.1 Process timings – Clinical Emergencies

Normally, Clinical Emergency notifications can be processed within one working day. This can be up to four calendar days or longer if the notification is received on a Friday afternoon or before a public holiday. Some notifications can take longer if there are queries, if a large number have been submitted, or if a medical assessment is required. Notifications originally submitted as non-emergencies may be processed as emergencies resulting from changes in circumstances. These will show as extended processing times. Graph 3 and Table 6 provide further information on timings.

Graph 3 Time to Issue Clinical Emergencies, 01 Jan 2015 to 31 Mar 2015

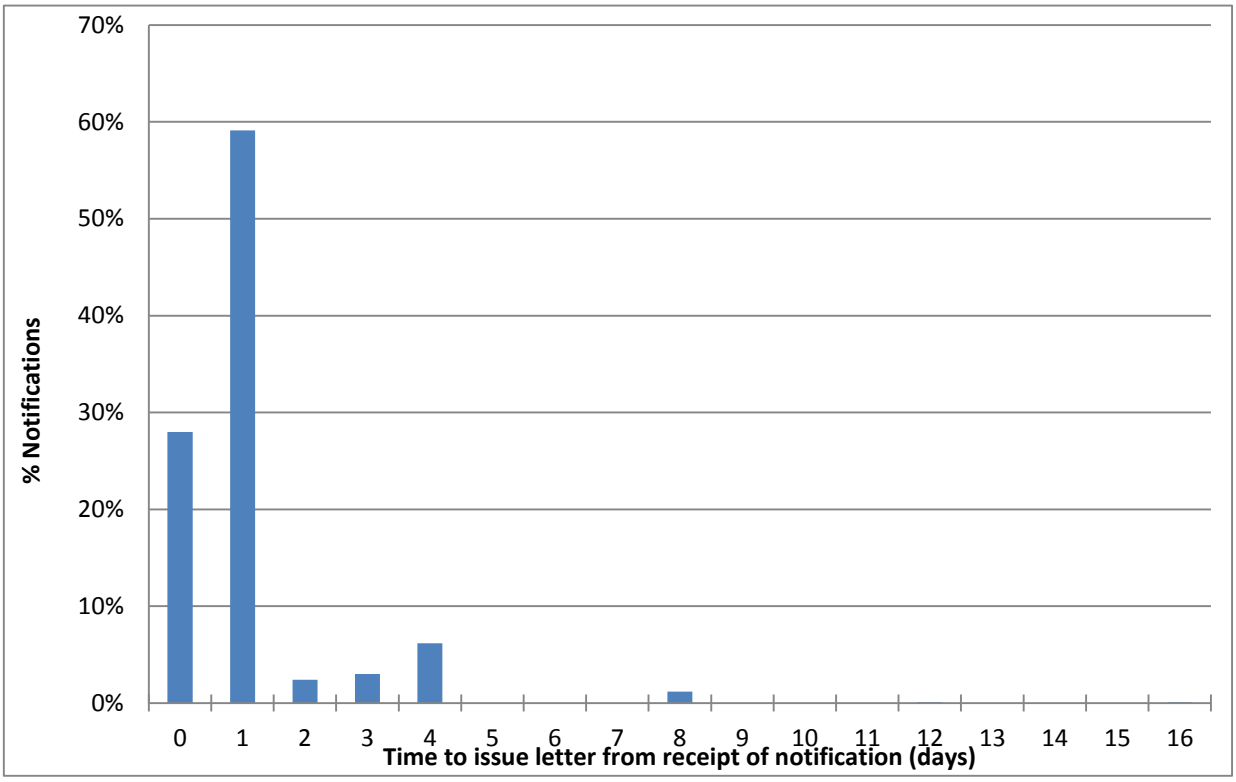


Table 6 Summary of Timings for Issuing Clinical Emergency Letters, 01 Jan 2015 to 31 Mar 2015

Time to Process from Receipt	Number of Notifications	% Notifications
% ≤ 4 days	1153	98.63%
% ≤ 1 day	1018	87.08%
Total Clinical Emergencies processed	1169	100%

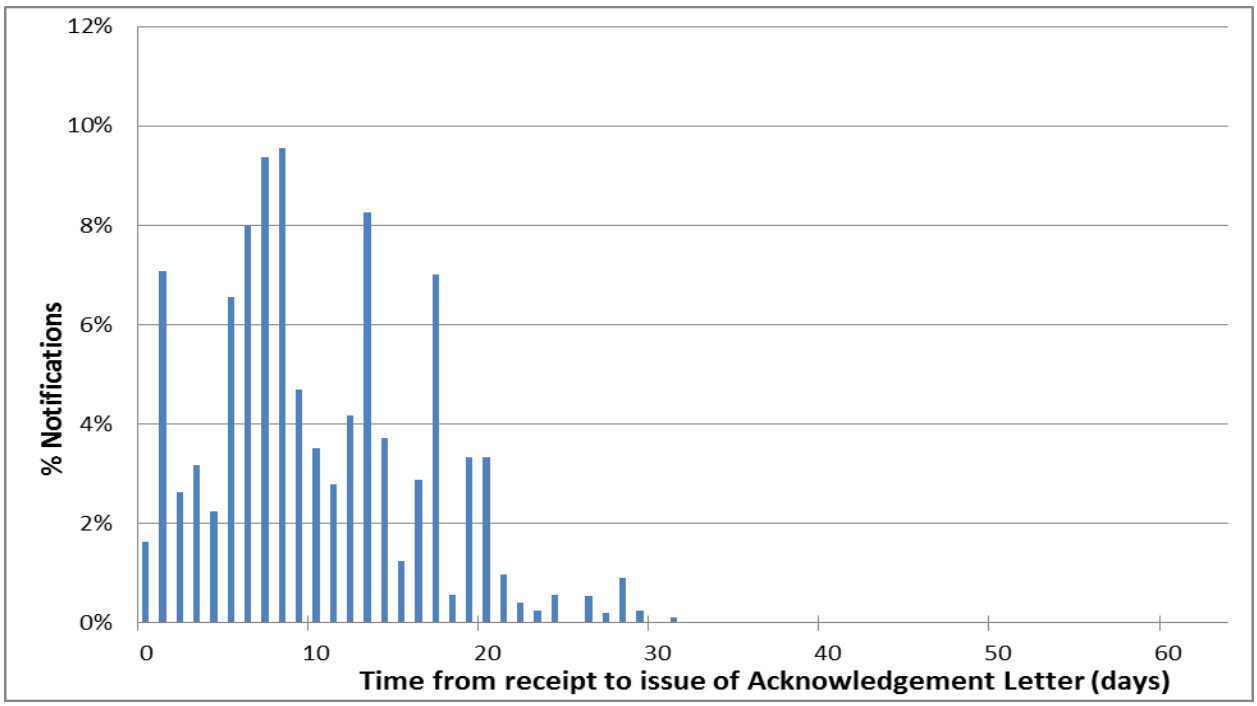
3.2 Process timings – Routine notifications

Graph 4 shows statistics for 8358 notifications for Q1/2015 where both received and acknowledgement letter issue dates are available and provides an estimate of the time taken to enter data onto the database after the received date of the notifications.

Significant delays can be experienced due to the necessity to obtain additional information from some importers to enable completion of data entry. Where spreadsheets have been submitted containing very large numbers of notifications there may also be delays due to the time taken to enter the data before acknowledgement letters can be issued.

Approximately 95% of acknowledgements were issued within 20 days of receipt of notifications.

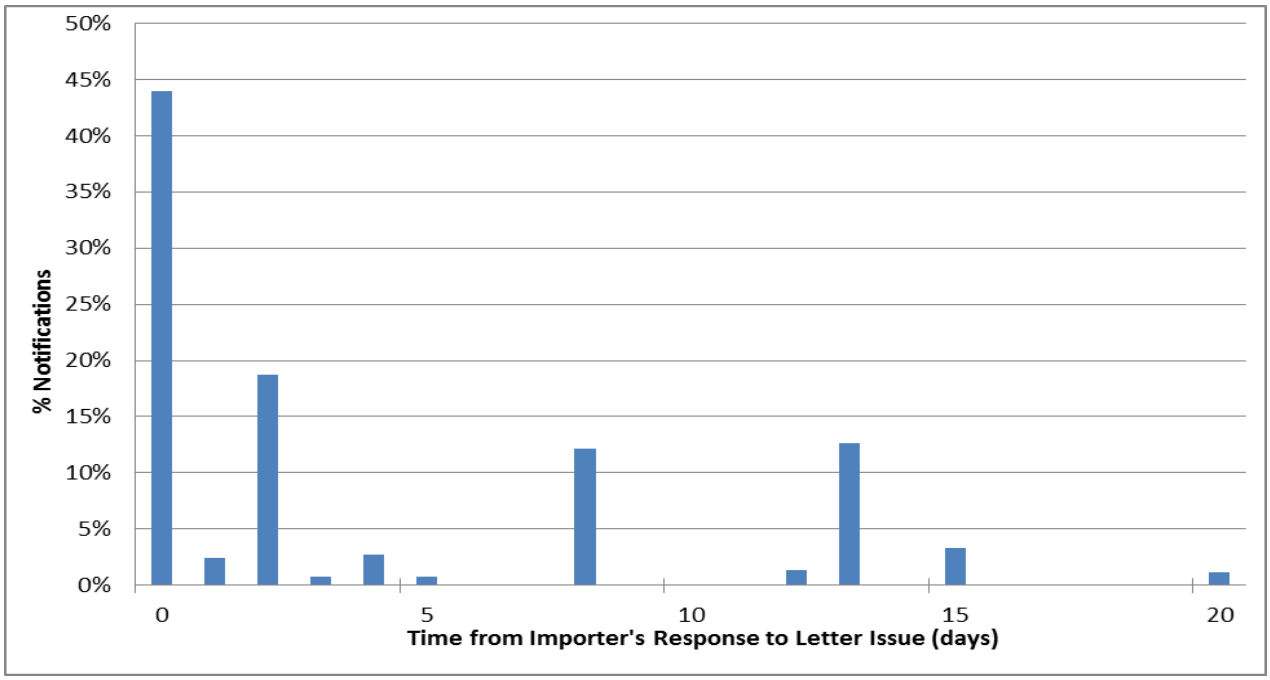
Graph 4 Time to issue Acknowledgements, 01 Jan 2015 to 31 Mar 2015



3.3 Process timings - Further information request responses

Importers responded to 666 requests for further information from the MHRA in Q1/2015 where letters permitting import were subsequently issued. Approximately 95% of these final letters were issued within 13 days of receiving the importer's response. See Graph 5.

Graph 5 Response times to further information provided, 01 Jan 2015 to 31 Mar 2015



3.4 Process timings – Objection letters

A total of 359 Objections with Reason letters were issued in Q1/2015. Of these, 218 were issued where acknowledgements had previously been issued. 7 notifications for import of a Centrally Authorised product were objected to beyond 28 days and subsequent regulatory action taken to ensure distribution ceased.

3.4.1 Summary of reasons for objections to import

Table 7 Reasons for objection to import

Summary	Number of notifications
Importer's licence not valid for activity	91
UK licensed product available	81
Excessive quantity over that permitted in SI 2012/1916	18
Centrally Authorised product available	17
Wrong licence number given by importer	6
GMP concerns	4

The most common reason for objecting to import in Q1 2015 was that the importer did not possess the correct licence. It is important for importers to understand that they require a Wholesale Dealer's Authorisation (WDA(H)) for import of unlicensed medicines from within the European Economic Area (EEA) and a Manufacturer's "Specials" Licence (MS) for importation of unlicensed medicines from outside the EEA. In each case the licence must be enabled for these activities.

Importers must also ensure they have robust procedures in place to check whether there is a licensed product available in the UK that can meet the clinical needs of the patient(s). No special clinical need exists if there is an equivalent licensed product available, and notifications for import

will attract objections unless there is a clinical reason why an apparently equivalent licensed product cannot be used.

Centrally Authorised products possess a Marketing Authorisation (”licence”) valid in all Member States and are NOT unlicensed medicines. They cannot be notified for import as unlicensed medicines. Unlicensed equivalents can only be considered for import where no centrally authorised product is available within the EEA.

When submitting notifications importers must observe the quantity restrictions in the regulations. It is also important to state the WDA(H) or MS number on the submission form. This must be the number of the importing company, NOT the number of a company that the importer is acting for.

A number of notifications attracted objections following requests for evidence of the manufacturer's compliance with EU GMP or equivalent in the form of a valid GMP Certificate issued following successful inspection of the manufacturing site for this or a similar product by a EU Member State or other PIC/S member. Certificates issued by local authorities, such as US or Indian States are not acceptable. Only certificates issued by the national authorities of PIC/S members will be accepted.

4 Inspection liaison

Information in the form of listings of unlicensed products notified for import together with background information including any significant issues is routinely provided to support site inspections of MS and WDA(H) holders and to assist Enforcement investigations. Nine inspections/Enforcement referrals were supported in Q1/2015 and a number of Inspectorate general queries answered.

5 Conclusions

The import notification system has operated substantially within the requirements of the regulations during Quarter 1, 2015.

There are concerns that objections to import have been issued because some importers do not fully understand the requirements of the regulations, especially in respect of the licence(s) required for importation of unlicensed medicines, and the conditions of those licenses.