



Summary Report for Importation of Unlicensed Medicines

01 Oct 2015 – 31 Dec 2015

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1 Introduction and summary

This report¹ covers the period 01-October-2015 to 31-December-2015 and shows the import notification system to be operating substantially within the requirements of SI 2012/1916.

¹ The data for this report were compiled on 23-March-2016 and reflect the Import Notification System at this date.

2 News and current issues

2.1 Centrally Authorised products

Occasionally shortages of Centrally Authorised products arise. At the time of writing, in Quarter 1, 2016, there is a shortage of Bexsero meningitis vaccine. This is a Centrally Authorised product with a Marketing Authorisation valid in all Member States.

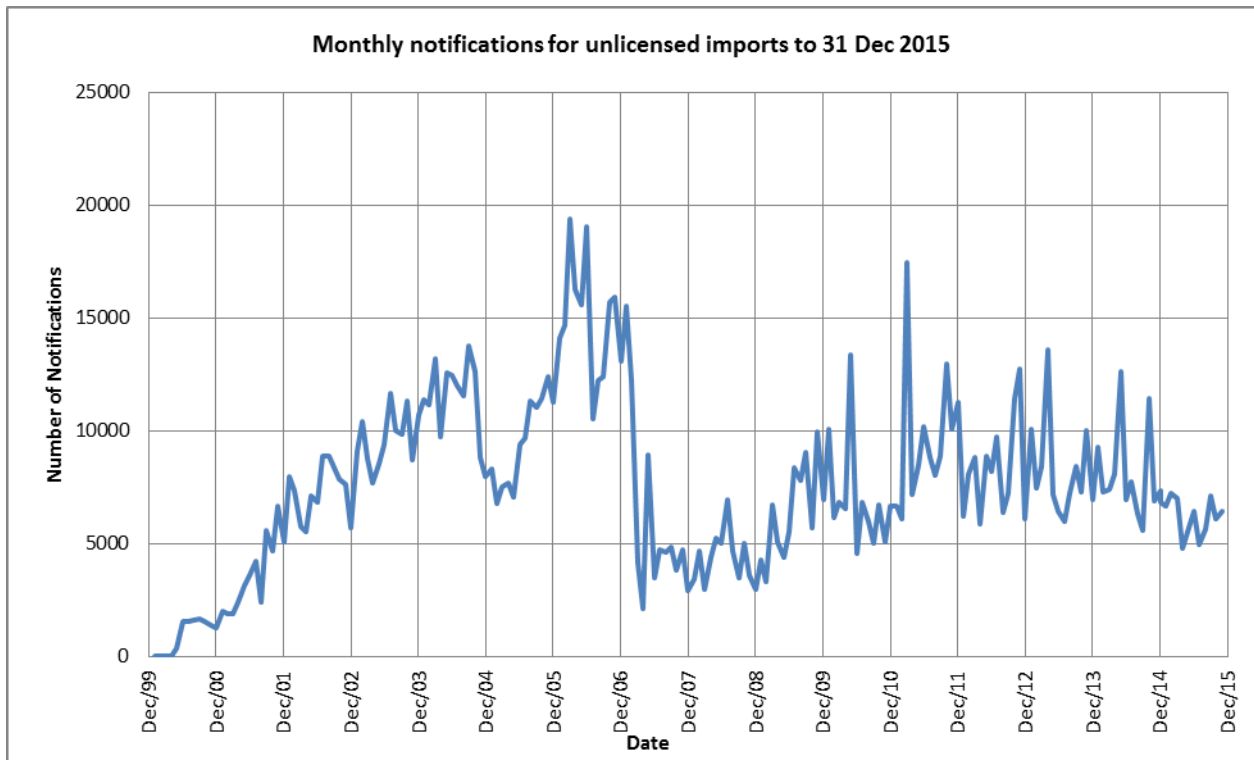
Some importers have enquired about notification of European Economic Area (EEA) sourced Bexsero for import as an unlicensed medicine. Products with Centrally Authorised marketing authorisations originating within the EEA are not unlicensed and may only be distributed by the Marketing Authorisation Holder or by way of Parallel Distribution following the European Medicines Agency (EMA) procedure. They cannot be notified for import as unlicensed medicines.

Objection is likely to be raised to import of unlicensed equivalents from outside the EEA unless the shortage is Europe wide, in which case the MHRA is happy to consider notifications for import of non-EEA unlicensed products, as is currently the case with Bexsero.

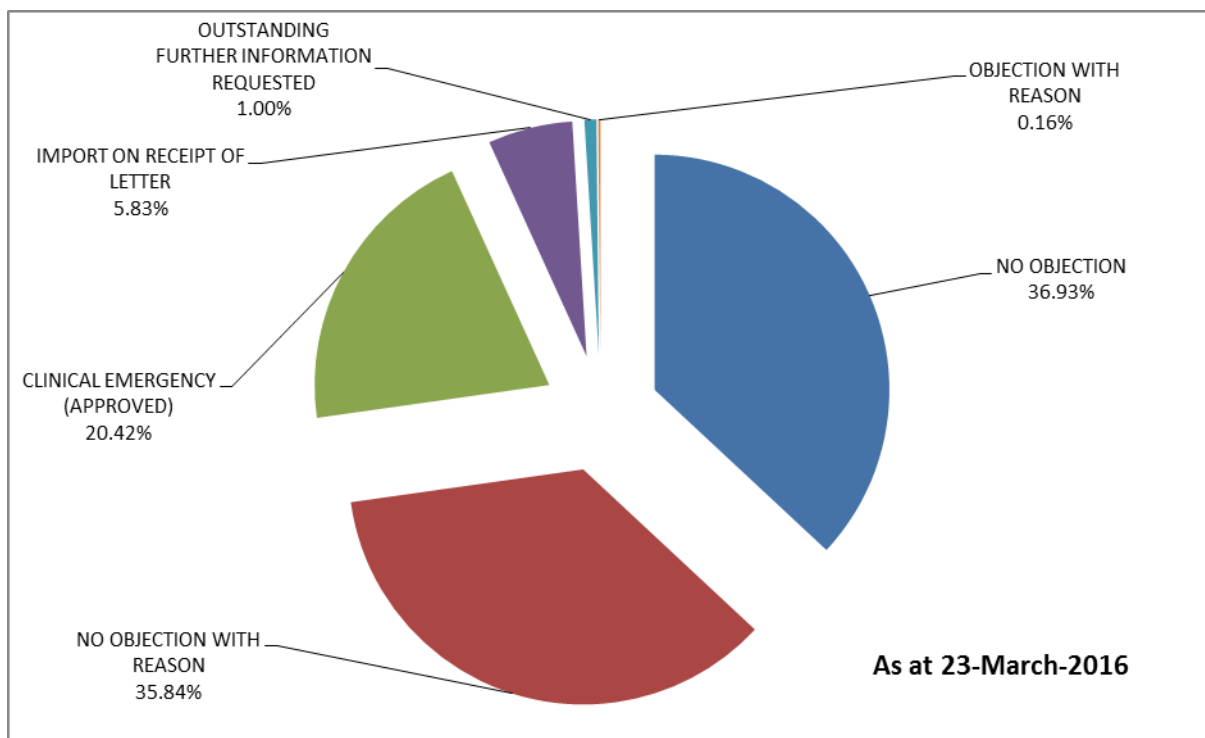
3 Notifications for importation

Graph 1 Monthly notifications for unlicensed imports

Note: Excludes invalid and cancelled notifications



Graph 2 Breakdown of valid notifications by status, 01 Oct – 31 Dec 2015



3.1 Importers

A total of 19609 notifications were received from 90 importers for the period 01 Oct 2015 to 31 Dec 2015. Of these, 6 importers accounted for approximately 75%.

Table 1 Valid notifications by importer 01 Oct 2015 to 31 Dec 2015

Importer Details	Number of Notifications	Percentage Share
90 Importers	19609	100%
Of which 6 importers		~74%

3.2 Countries of export of products

Table 2 Countries of export 01 Oct 2015 to 31 Dec 2015

Rank	Exporting Country	Number of Notifications	% Share
1	Germany	4820	24.58%
2	United States of America	2810	14.33%
3	Australia	2755	14.05%
4	France	1750	8.92%
5	Canada	1479	7.54%
6	Italy	1470	7.50%
7	Spain	977	4.98%
8	Switzerland	490	2.50%
9	The Netherlands	448	2.28%
10	Belgium	383	1.95%
11	Denmark	277	1.41%
12	Lithuania	265	1.35%
13	Hungary	238	1.21%
14	India	183	0.93%
15	Republic of Ireland	172	0.88%
16	Poland	162	0.83%
17	Austria	148	0.75%
18	Romania	128	0.65%
19	Czech Republic	116	0.59%
20	Japan	116	0.59%
21	New Zealand	113	0.58%
22	Norway	96	0.49%
23	Latvia	92	0.47%
24	Sweden	45	0.23%
25	Portugal	24	0.12%
26	Finland	20	0.10%
27	Slovakia	16	0.08%
28	Singapore	8	0.04%
29	Puerto Rico	3	0.02%

Rank	Exporting Country	Number of Notifications	% Share
30	South Africa	3	0.02%
31	Greece	1	0.01%
32	Russia	1	0.01%
	Sum:	19609	100.00%
	EEA	11648	59.40%
	Non-EEA	7961	40.60%

3.3 Most frequently notified products

Table 3 Top 50 frequently notified products 01 Oct 2015 to 31 Dec 2015

Rank	Product Name	Number of Notns	% all Notns
1	Haloperidol Injections 5mg/ml	2389	12.18%
2	Co-Proxamol 32.5mg/325mg Tablets	2172	11.08%
3	Thyroid Oral Preps	732	3.73%
4	Homoeopathics	724	3.69%
5	Melatonin Tablets and Capsules, All Strengths	525	2.68%
6	Co-Trimoxazole Inj/Inf 480mg/5ml	506	2.58%
7	Vitamins - Oral Preps	434	2.21%
8	Benzathine Penicillin Injections All Strengths	408	2.08%
9	Bisacodyl Enema 10mg/30ml	399	2.03%
10	Allergy Tests	364	1.86%
11	Sodium Chloride Ophthalmic Preps (Ointments & Eyedrops)	335	1.71%
12	Cyclosporin Ophthalmic Ointments & Eyedrops	301	1.54%
13	Sucralfate Tablets and Oral Suspensions	287	1.46%
14	Tretinoin/Vitamin A with and without Hydroquinone Topicals (Creams Oints., Gels Etc.)	275	1.40%
15	Carfilzomib 60 mg Lyophilized Inj	239	1.22%
16	Pristinamycin 500mg Tablets	228	1.16%
17	Evofosfamide 100mg/ml Con. For Sol For Infus	220	1.12%
18	Talc For Pleurodesis	214	1.09%
19	Lu-Dota, Tyr Ocfreotate, Lutetium-177 (177 Lu) Labelled	208	1.06%
20	Adrenaline Injection, 1:10,000 Syringe 1mg/10ml	200	1.02%
21	Flunarizine Tablets & Capsules, All Strengths	199	1.01%
22	Pirenzepine 50mg Tablets	187	0.95%
23	Progesterone 100mg/1ml Injections	186	0.95%
24	Cyclizine Injections 50mg/ml	179	0.91%
25	Idebenone 45mg Tablets & Capsules	161	0.82%
26	Povidone-Iodine 50 mg/ml Soln For Inj	156	0.80%
27	Fumaric Acid Esters 30 & 120mg Tablets	154	0.79%
28	Mexiletine Capsules All Strengths	152	0.78%
29	Ketamine Injections	136	0.69%
30	L-Ornithine L-Aspartate Sachets/3000mg	136	0.69%
31	Betamethasone Injections All Strengths & Salts	134	0.68%
32	Bacillus Calmette-Guerin (BCG) Vaccines & Instillations	132	0.67%
33	Lacosamide 50 mg Tabs	128	0.65%
34	Acetylcysteine Oral Preparations (Tablets, Granules Etc.)	116	0.59%
35	Thioridazine Tablets All Strengths	116	0.59%
36	Triamcinolone Acetonide, Neomycin Sulfate, Nystatin, Gramicidin Ear Ointment	109	0.56%
37	Aspirin 300mg Suppositories	98	0.50%
38	Sultiame Tablets All Strengths	97	0.49%
39	Diazoxide 50mg/ml Oral Suspension	96	0.49%
40	Emtricitabine/Tenofovir Tablets, Various Dose Combinations	96	0.49%

Rank	Product Name	Number of Notns	% all Notns
41	Isoprenaline 0.2 mg/ml Injections	96	0.49%
42	Allergy Treatments (SCIT & SLIT)	95	0.48%
43	Pentosan Polysulfate 50 & 100mg Capsules	95	0.48%
44	Insulin, Human Injections All Strengths	90	0.46%
45	Dimethyl Sulfoxide 50% Intravesical Instln Solutions	88	0.45%
46	Doxycycline 100mg/5ml Sol For Inj	85	0.43%
47	Indigo Carmine 4mg/ml Inj	83	0.42%
48	Ranitidine 25 mg/ml Injection	80	0.41%
49	Chlorothiazide Tablets & Suspensions	76	0.39%
50	Vitamins, Parenteral	71	0.36%

3.4 Vaccines and immunoglobulins

Table 4 Vaccines & immunoglobulins 01 Oct 2015 to 31 Dec 2015

Rank	Product Name	Number of Notifications
1	Bacillus Calmette-Guerin (BCG) Vaccines & Instillations	132
2	Typhoid Vaccine (VI Capsular Polysaccharide) 25 mcg/0.5 ml Injection Soln	11
3	Tuberculin PPD	8
4	Antithymocyte Immunoglobulin (Horse) 50mg/ml	7
5	Zn-DTPA Sol For Infusion	5
6	DTAP/IPV	4
7	DTAP/IPV/HIB	4
8	Anti Human-T-Lymphocyte Immunoglobulin 20mg/ml	1
9	CMV Immunoglobulin 5% Infn Soln 100iu/ml	1
10	Diphtheria Antitoxin 500U/ml	1
11	IgM Enriched Normal Human Immunoglobulin Solution For Infusion 5%	1
12	Measles Vaccine (Live) Pow/Solv For Inj	1
13	Polio Vaccine Inactivated	1
14	Refined Equine Anti- <i>Echis carinatus /ocellatus</i> Venom Immunoglobulins (<i>Echis carinatus</i> Antivenom)	1

3.5 Shortages

Table 5. Products notified claiming UK product shortages, 01 Oct 2015 to 31 Dec 2015

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

Product Name	Number of Notifications
Haloperidol Injections 5mg/ml	2191
Co-Trimoxazole Inj/Inf 480mg/5ml	506
Sucralfate Tablets and Oral Suspensions	285
Adrenaline Injection, 1:10,000 Syringe 1mg/10ml	200
Cyclizine Injection 50mg/ml	179
BCG Instillations and Vaccines	132

Product Name	Number of Notifications
Ketamine 100mg/ml Injections	124
Betamethasone 4mg/1ml Injections	105
Levothyroxine Tablets All Strengths	85
Potassium Chloride 600 mg SR Tabs& Caps	70
Iobitriodol 300mg Iodine Per ml Vials	60
Co-Phenotrope 2.5 mg/25 mcg Tablets	59
Liothyronine 20& 25 mcg Tablets	46
Melphalan 50mg Injections	30
Vecuronium Injections 10mg	30
Testosterone Ampoules/100mg In 2ml	29
Disulfiram 500 mg Tablets	22
Demeclocycline Tabs 150mg	21
Primaquine 7.5 mg Tablets	20
Lidocaine HCl Inj, 2%, Syringe, 100mg/5ml	12
Sodium Bicarbonate Inj 8.4% Syringe 50mEq/50ml	12
Metoclopramide Hcl 5mg/ml Sol For Inj/Inf	8
Promethazine 50mg/2ml Injection Solution	8
Suxamethonium 2% Injection Soln	8
Tuberculin PPD 5iu/0.1ml Injection Soln	8
Potassium Canrenoate 250mg/10ml Injection	5
Ribavirin 6g/Vial Powder For Inhalation Sol	5
Aspirin Suppositories 300mg	4
DTAP/IPV vaccine	4
DTAP/IPV/HIB vaccine	4
Hyoscine 0.3 mg Chewable Tablets	4
Megestrol 160mg Tabs	4
Nefopam 30mg Tablets	4
Clonidine Hydrochloride 150 mcg/ml Sol For Inj/Infus	3
Trifluoperazine 1 mg Tablets	3
Etoposide 100mg/5ml Conc For Infn Soln	2
Hydrocortisone Sodium Succinate 100mg Vials	2
Sulfinpyrazone Tablets 200mg	2
Fomepizole Injections/Infusions	2
Sulfinpyrazone 250 mg Tablets	1
Amino Acid Solution (Infant) For Infusion	1
Aspirin Powder & Solv For Soln For Inj 1g Vials	1
Chloramphenicol Sodium Succinate 1 G Powder For Inj	1
Cidofovir 375 mg/5ml Infusion Soln	1
Dibotermin Alfa 12 mg Kit For Implant	1
Edrophonium Chloride 10mg/ml Injection	1
Gentamicin Sulphate (Septopal Chain)	1
Labetalol100mg/20ml Sln For Inj/Inf	1
Triamcinalone Acetonide 10mg/ml Inj Susp	1
Vasopressin 20units/ml Inj Soln	1

4 Administrative matters

4.1 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 urgently 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 Oct 2015 to 31 Dec 2015

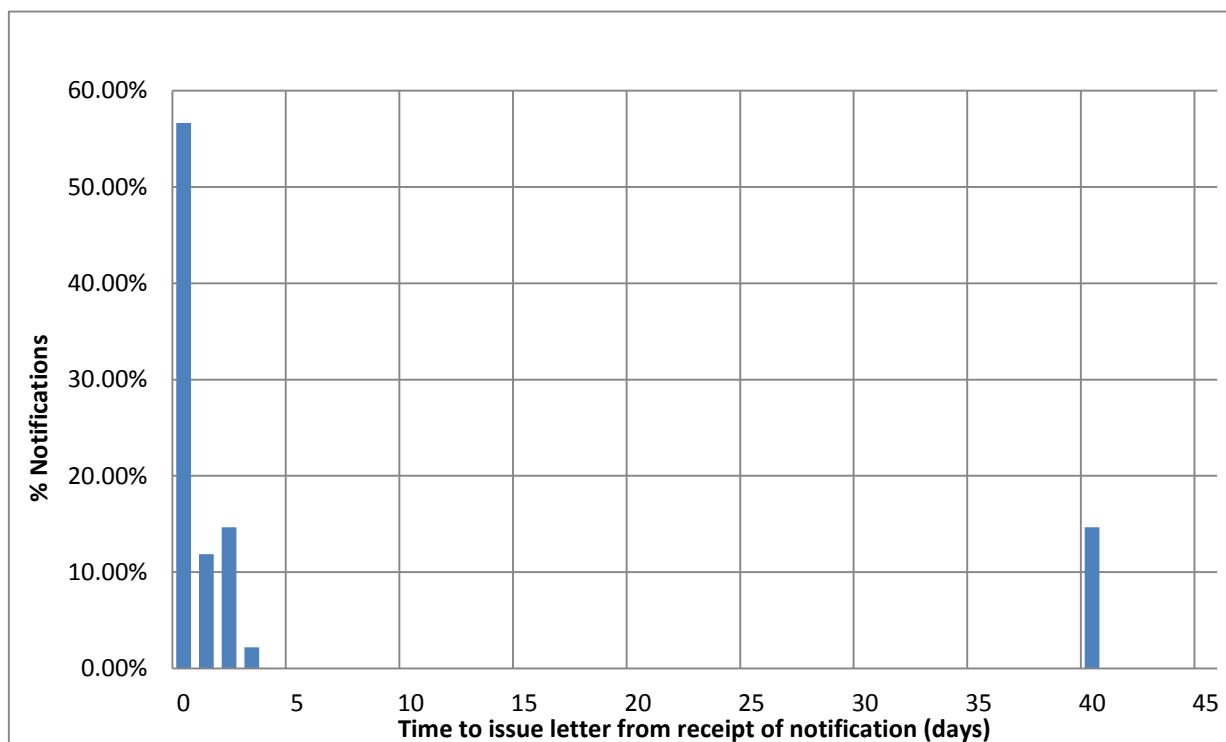


Table 6 Clinical Emergency Letter Timings, 01 Oct 2015 to 31 Dec 2015

Time to Process from Receipt	Number of Notifications	Comments
≤ 1 day	935	68.50% issued within 1 day
≤ 3 days	1165	85.45% issued with 3 days
Totals	1365	

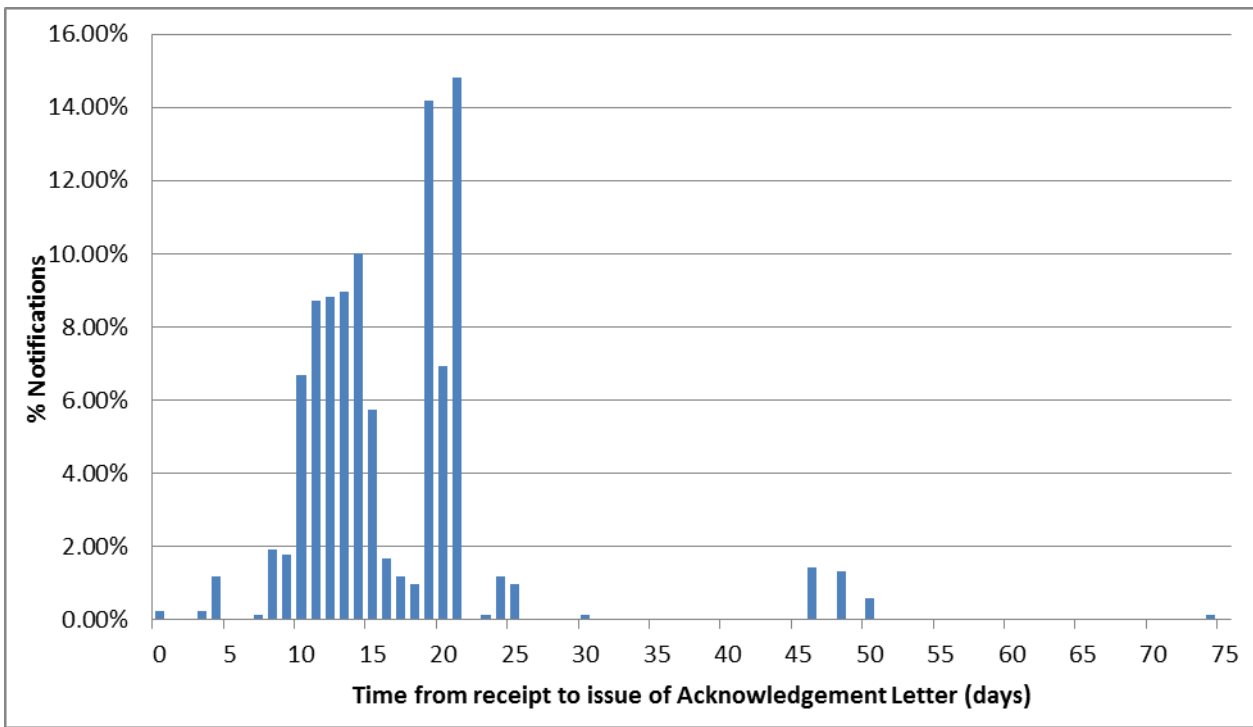
4.2 Process timings – Routine notifications

Graph 4 shows statistics for 838 notifications for Q4/2015 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 24 days of receipt of notifications.

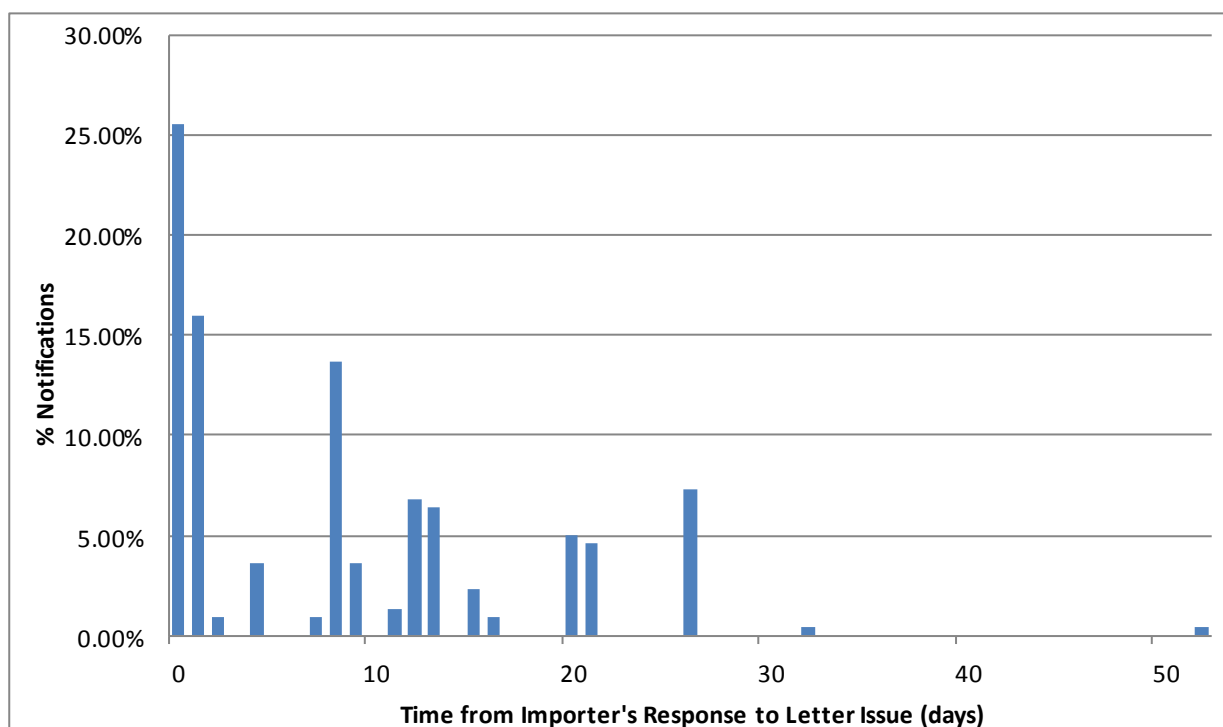
Graph 4 Time to issue Acknowledgements, 01 Oct 2015 to 31 Dec 2015



4.3 Process timings - Further information request responses

Importers responded to 219 requests for further information from the MHRA in Q4/2015 where letters permitting import were subsequently issued. Approximately 79% of these final letters were issued within 14 days of receiving the importer’s response. See Graph 5.

Graph 5 Response times to further information provided, 01 Oct 2015 to 31 Dec 2015



4.4 Process timings – Objection letters

A total of 31 Objections with Reasons were issued in Q4/2015. Of these, 3 were issued where acknowledgements had previously been issued. Each of these Objection with Reason letters was issued within 28 days of acknowledgement.

4.4.1 Summary of reasons for objections to import

Table 7 Reasons for objection to import

Summary	Number of notifications
No special need: importer actually stated that they were aware of an available UK licensed product. Also countries of manufacture were not provided.	22
Centrally Authorised product available	3
Importer's licence not valid for activity	2
Lactose free product requested, but UK licensed product was in fact lactose free	1
Shortage of UK product claimed, but there was no shortage	1
Equivalent UK licensed product available	1
Safety concerns	1

Unlicensed medicines must not be supplied if there is an equivalent licensed product available that can meet the patient's clinical needs. This may be a UK licensed product available within the UK or a Centrally Authorised product available within the EEA.

Importers are reminded that importation of unlicensed medicines requires a Wholesale Dealer's Authorisation (WDA(H)) for import from within the EEA and a Manufacturer's "Specials" Licence (MS) for import from outside the EEA. In each case the licence must be enabled to permit this

activity by specifically selecting the appropriate options when applying for the licence, or by requesting a variation to add these options.

Importers are also reminded that where the supplier is not the manufacturer, they must inform the MHRA of the supplier's details when notifying.

5 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. Five inspections were supported in Q4/2015 and a number of Inspectorate and Enforcement general queries answered. The Pharmaceutical Assessor for imported unlicensed medicines was pleased to attend two inspections in person to provide advice and support.

6 Conclusions

The import notification system has operated substantially within the requirements of the regulations during Quarter 4, 2015.