Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

Summary Report for Importation of Unlicensed Medicines

01 Jan 2016 – 31 Mar 2016

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Contents

1 Introduction and summary

This report[1] covers the period 01-Jan-2016 to 31-Mar-2016 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 in November 2016 and reflect the Import Notification System at this date.

2 News and current issues

Once again objections to notifications for import of unlicensed medicines have been issued for notifications for Centrally Authorised medicine with Marketing Authorisations valid throughout the EEA.

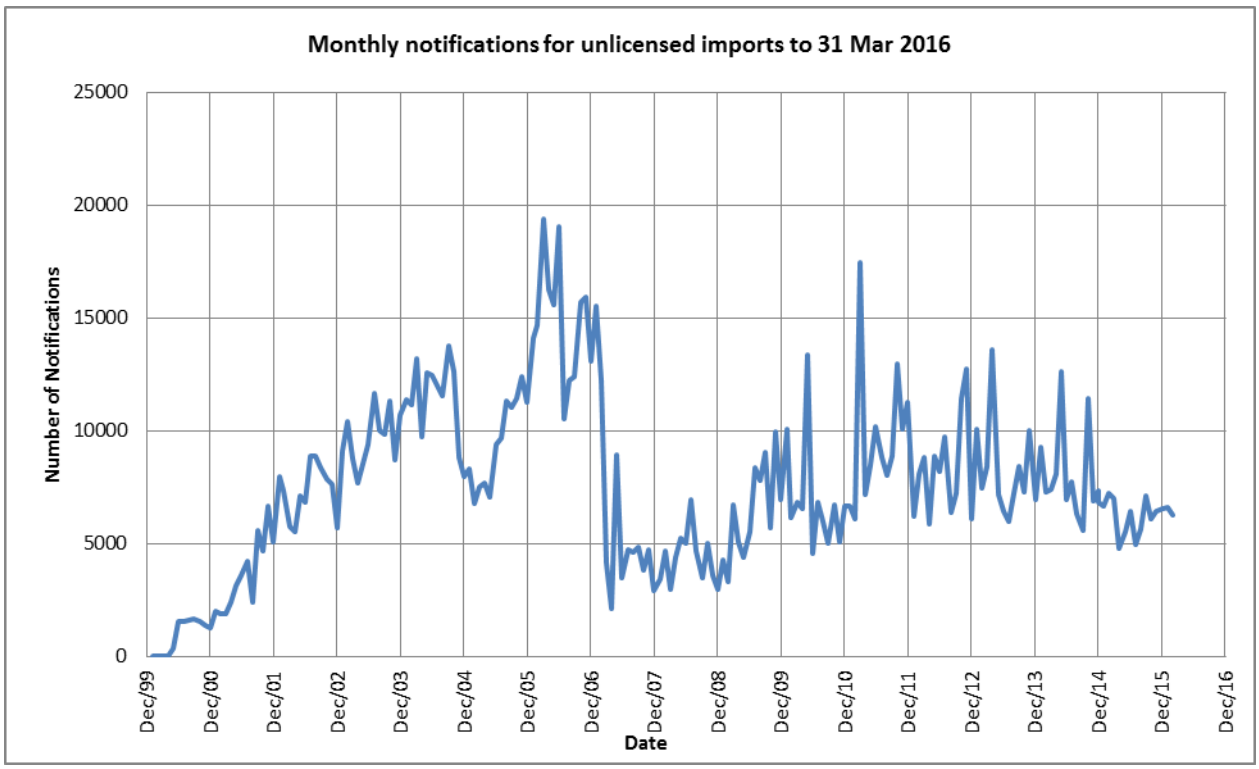
Unlicensed medicines must not be supplied if there is an equivalent licensed product available that can meet the patient’s clinical needs. This may be a UK licensed product available within the UK or a Centrally Authorised product available within the EEA.

Also a number of objections to import have been issued due to lack of assurances of product quality. To ensure imported unlicensed medicines comply with acceptable Good Manufacturing Practices the MHRA may request 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 the notified product or a similar product by a EU Member State or other PIC/S member. Evidence originating from non-PIC/S members will not be acceptable.

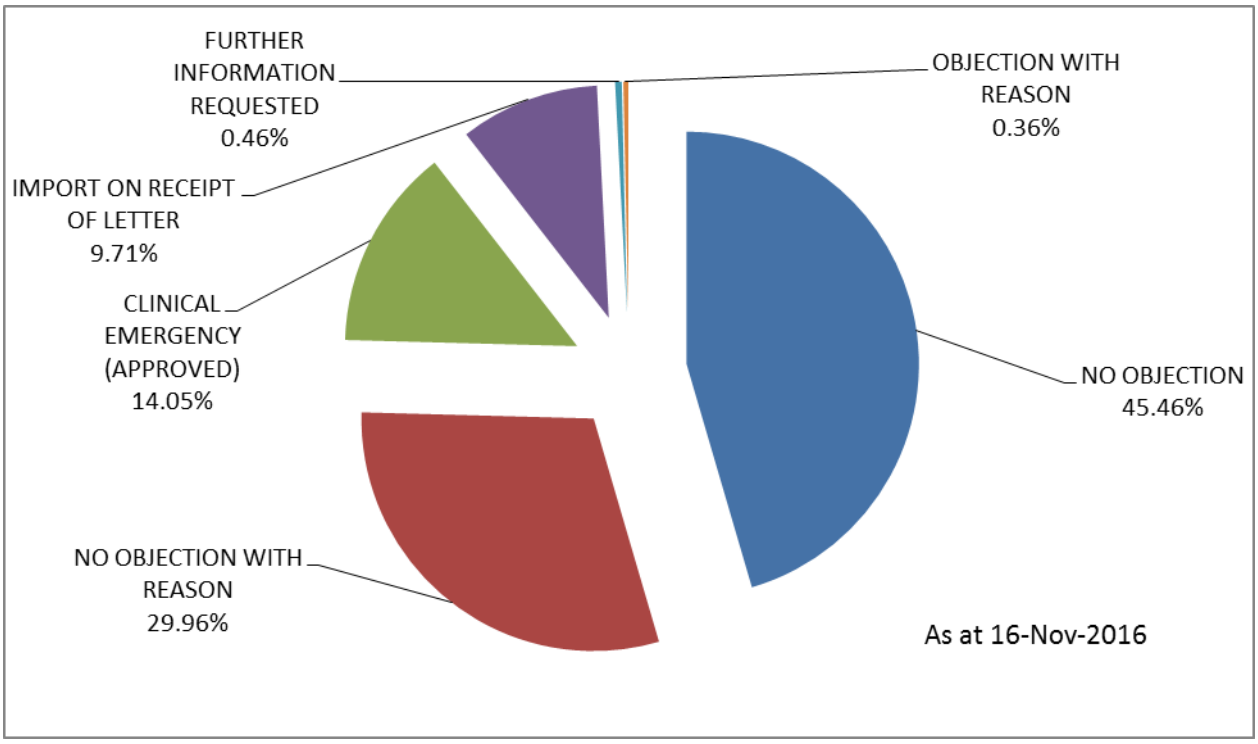
3 Notifications for importation

Graph 1 Monthly notifications for unlicensed imports

Note: Excludes invalid and cancelled notifications



Graph 2 Breakdown of valid notifications by status, 01 Jan – 31 Mar 2016



3.1 Importers

A total of 19414 notifications were received from 86 importers for the period 01 Jan 2016 to 31 Mar 2016. Of these, 7 importers accounted for approximately 75%.

Table 1 Valid notifications by importer 01 Jan 2016 to 31 Mar 2016

Importer Details	Number of Notifications	Percentage Share
86 Importers	19414	100%
Of which 7 importers	13539	~75%

3.2 Countries of export of products

Table 2 Countries of export 01 Jan 2016 to 31 Mar 2016

Rank	Exporting Country	Number of Notifications	% Share
1	Germany	3885	20.01%
2	United States of America	3666	18.88%
3	Italy	2531	13.04%
4	Spain	1622	8.35%
5	France	1439	7.41%
6	Canada	1408	7.25%
7	Australia	1273	6.56%
8	The Netherlands	369	1.90%
9	Switzerland	359	1.85%
10	India	304	1.57%
11	Sweden	261	1.34%
12	Belgium	854	4.40%
13	Denmark	203	1.05%
14	New Zealand	203	1.05%
15	Austria	180	0.93%
16	Poland	156	0.80%
17	Republic Of Ireland	107	0.55%
18	Norway	89	0.46%
19	Czech Republic	78	0.40%
20	Hungary	67	0.35%
21	Portugal	60	0.31%
22	Japan	56	0.29%
23	Finland	54	0.28%
24	Greece	41	0.21%
25	Cyprus	40	0.21%
26	Romania	40	0.21%
27	Lithuania	24	0.12%
28	South Korea	22	0.11%
29	Slovak Republic	14	0.07%
30	Thailand	3	0.02%
31	United Kingdom*	3	0.02%

Rank	Exporting Country	Number of Notifications	% Share
32	Saudi Arabia	2	0.01%
33	Israel	1	0.01%
	Sum:	**19414**	100.00%
	EEA	**12117**	62.41%
	Non-EEA	**7297**	37.59%

*UK is not an acceptable exporting country!

3.3 Most frequently notified products

Table 3 Top 50 frequently notified products 01 Jan 2016 to 31 Mar 2016

Rank	Product name	Number of Notns	% all Notns
1	Allergy tests	1093	5.63%
2	Homoeopathics	868	4.47%
3	Fluphenazine injections, all strengths	809	4.17%
4	Saline injections/infusions	716	3.69%
5	Fumaric acid esters 30 &120mg tablets	576	2.97%
6	Thyroid oral preps	555	2.86%
7	Sucralfate oral preparations (tabs, susp)	529	2.72%
8	Ranitidine 25 mg/ml - sol for inject	520	2.68%
9	Bisacodyl enema 10mg/30ml	461	2.37%
10	Melatonin tablets and capsules, all strengths	455	2.34%
11	Vitamins - oral preps	425	2.19%
12	Acetylcysteine oral preparations (tablets, granules etc.)	332	1.71%
13	Cyclizine 50mg/ml injections	308	1.59%
14	Potassium chloride 600mg controlled release tablets	303	1.56%
15	Daratumumab inj/infn solutions	279	1.44%
16	Meningococcal group b vaccine (rDNA,multi component,adsorbed) suspension for injection	264	1.36%
17	Pirenzepine 50mg tablets	244	1.26%
18	Ibrutinib 140 mg capsules	240	1.24%
19	Pristinamycin 500mg tablets	240	1.24%
20	Procaine penicillin injections all strengths	221	1.14%
21	Cidofovir injections/infusions	214	1.10%
22	Budesonide inhalation products	209	1.08%
23	Lu-dota, tyr ocfreotate, lutetium-177 (177 Lu) labelled	208	1.07%
24	Indigocarmine injections all stengths	207	1.07%
25	Povidone-iodine 5% ophthalmic solutions	202	1.04%
26	Fosfomycin oral preparations	196	1.01%
27	Benzathine penicillin injections all strengths	182	0.94%
28	Co-trimoxazole 480mg/5ml injections/infusions	181	0.93%
29	Co-proxamol tablets	180	0.93%
30	Human chorionic gonadotrophin 5000 iu vials	180	0.93%
31	Haloperidol 5mg/ml injections	170	0.88%
32	Metolazone tablets 2.5 & 5mg	169	0.87%
33	Triamcinolone acetonide, neomycin sulfate, nystatin, gramicidin ear ointment	161	0.83%
34	Levoketoconazole 150mg tablets	160	0.82%
35	Benzbromarone 100mg	157	0.81%
36	Flunarizine tablets & capsules, all strengths	144	0.74%

Rank	Product name	Number of Notns	% all Notns
37	Phentolamine injections	143	0.74%
38	Cyclosporin ophthalmic preparations	141	0.73%
39	Ixazomib tablets all strengths	136	0.70%
40	Probenecid 250 & 500mg tablets	135	0.70%
41	Iloprost 50 & 100mcg injections	134	0.69%
42	L-ornithine L-aspartate 3000mg sachets	131	0.67%
43	Pentosan polysulfate 50 & 100mg caps	119	0.61%
44	Progesterone injections all strengths	119	0.61%
45	Betamethasone 4mg/1ml injections	118	0.61%
46	Tretinoin/Vitamin A with and without hydroquinone topicals (creams oints., gels etc.)	113	0.58%
47	Diazoxide orals preps (capsules, suspension)	108	0.56%
48	Megestrol acetate oral preps all strengths	108	0.56%
49	Vitamins- parenteral preps	102	0.53%
50	Demeclocycline tablets 150mg	99	0.51%

3.4 Vaccines and immunoglobulins

Table 4 Vaccines & immunoglobulins 01 Jan 2016 to 31 Mar 2016

Rank	Product Name	Number of Notifications
1	Meningococcal group B vaccine (RDNA,multi component,adsorbed)	264
2	Antithymocyte globulin - equine	44
3	Tetanus, diphtheria, pertussis and polio vaccine	12
4	Diphtheria+tetanus+acellular pertussis+inactivated poliomyelitis+haemophilus influenza type B conjug	10
5	Human papillomavirus 9-valent vaccine, recombinant	8
6	Tuberculin PPD	8
7	Bacillus calmette guerin (BCG)	7
8	Polio vaccine inactivated	3
9	Tetanus toxoid adsorbed	3

3.5 Shortages

Table 5. Products notified claiming UK product shortages, 01 Jan 2016 to 31 Mar 2016

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

Product name	Number of Notifications
Fluphenazine injections	628
Cyclizine injection 50mg/ml	307
Potassium chloride SR 600mg Tablets	303
Sucralfate 1g tablets	291
Sucralfate 1g/5ml (20%) oral susp	219
Budesonide inhalations	208
Co-trimoxazole 480mg/5ml injection	181
Human chorionic gonadotrophin 5000 iu vials	180
Haloperidol 5mg/ml injection	170

Product name	Number of Notifications
Demeclocycline 150mg tablets	99
Phentolamine inj soln 5mg/ml	86
Betamethasone 4mg/ml injections	62
Megestrol acetate 160mg tabs	40
Verapamil hydrochloride 180mg sustained release tablets	30
Rifampicin 600mg pdr/solv injection/infusion	29
Levomepromazine 25mg/ml injections	28
L-Thyroxine 25 &50 mcg tabs	26
Liothyronine 20 & 25 mcg tablets	23
Melphalan 50mg iv infusion	20
Co-phenotrope tablets	18
Ketamine 100mg/1ml injections	18
Vasopressin sln for inj 20u/ml	16
Tetanus, diphtheria, pertussis and polio low dose TDAP/IPV 0.5ml PFS	12
Trifluoperazine hydrochloride 1 mg tablets	10
Carmustine 7.7mg implant	9
Disulfiram 250mg & 500 mg tablets	9
Perphenazine tablets 2 & 4mg	9
Progesterone 50& 100mg/ml injections	9
Aztreonam injection 1 g	8
Fomepizole 1g/ml infn soln	8
Hydrocortisone sodium succinate100mg lyophilisate solv/sol inj/inf 1x1	8
Sulfinpyrazone 200mg tablets	7
BCG vaccines	6
Tuberculin PPD 5iu/0.1ml injection soln	6
Edrophonium 10mg/ml injection	5
Chlortalidone 50mg tabs	4
Lorazepam 2 mg/ml injection	4
Promethazine hydrochloride injection 50mg/2 ml	4
Atracurium 50mg/5ml injections	3
Ribavirin for inhalation soln 6g	3
Vecuronium bromide 10mg injection	3
Clonidine hydrochloride 150 mcg/ml sol for inj/infus	2
Hyoscine 1.54 mg transdermal patch	2
Potassium canrenoate 250mg/10ml injection	2
Acetazolamide 250 mg scored tablets	1
Amino acid solution for infants, infusion	1
Succimer 200mg capsules	1
Testosterone undecanoate capsules 40mg	1
Thiopental sodium 1000mg powder for solution for inj	1
Triamcinalone acetonide 10mg/l inj susp	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 Jan 2016 to 31 Mar 2016

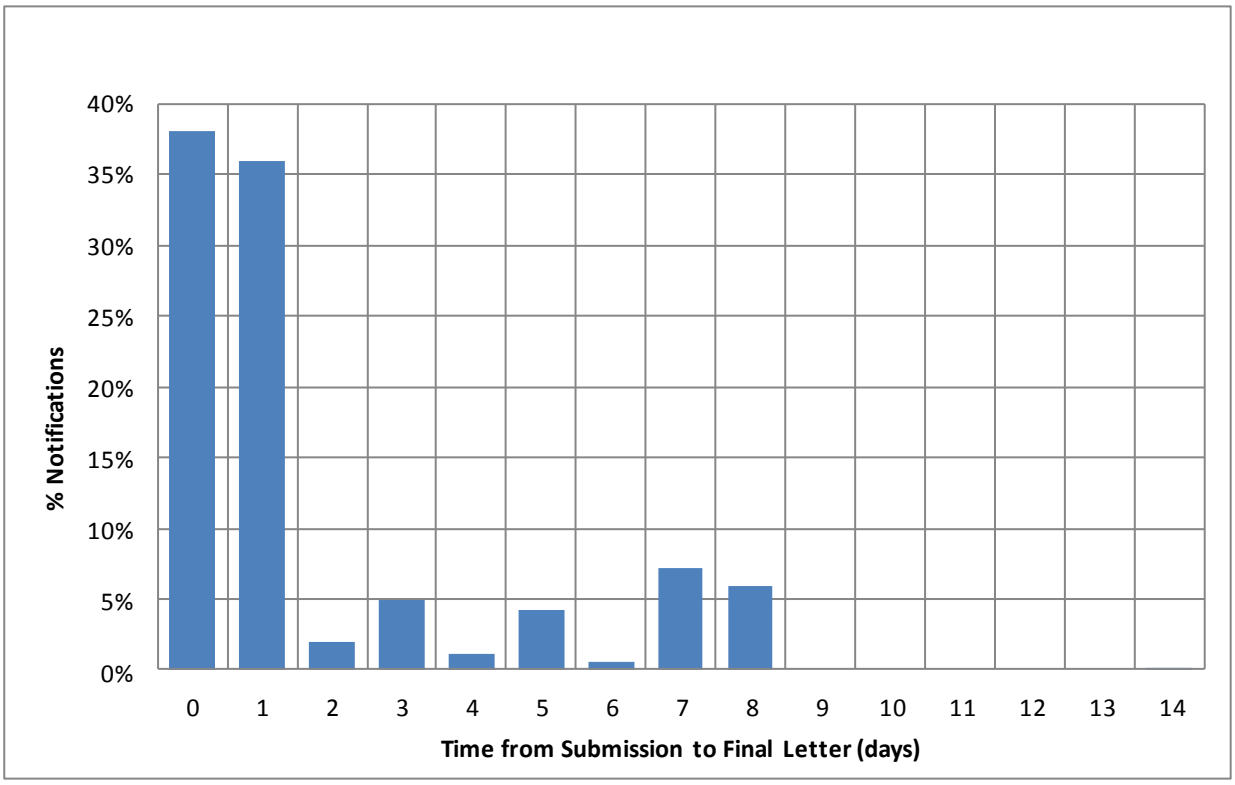


Table 6 Clinical Emergency Letter Timings, 01 Jan 2016 to 31 Mar 2016

Time to Process from Receipt	Number of Notifications	% Notifications
≤ 1day	2019	74.01% issued within 1 day
≤ 3 days	2207	80.9% issued within 3 days
Totals	**2729**	**100%**

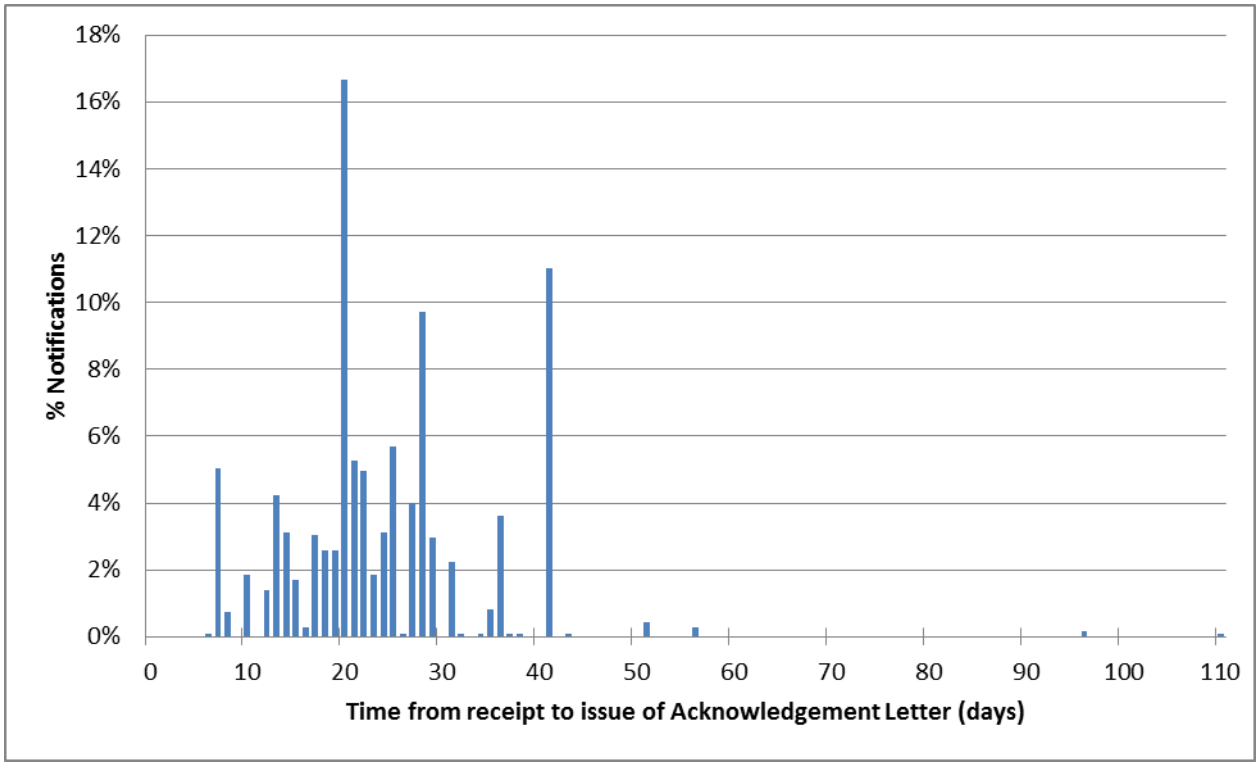
4.2 Process timings – Routine notifications

Graph 4 shows statistics for 1350 notifications for Q1/2016 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 80% of acknowledgements were issued within 30 days of receipt of notifications.

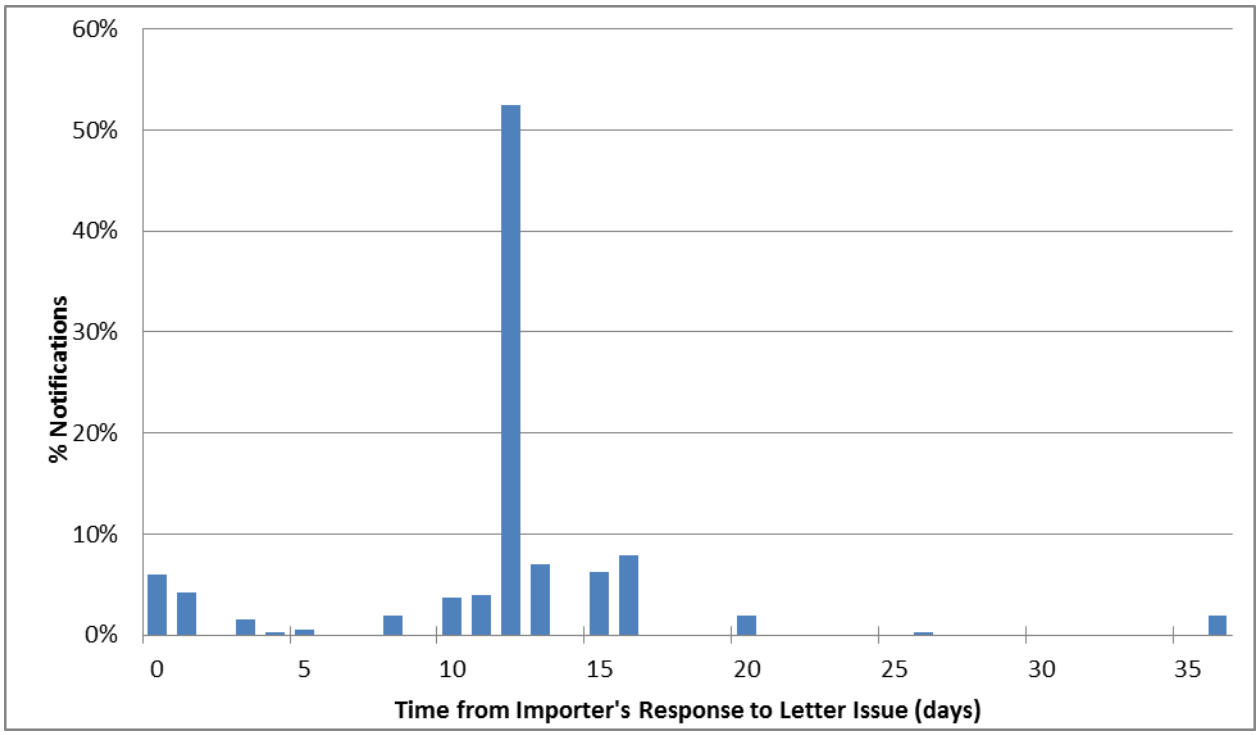
Graph 4 Time to issue Acknowledgements, 01 Jan 2016 to 31 Mar 2016



4.3 Process timings - Further information request responses

Importers responded to 402 requests for further information from the MHRA in Q1/2016 where letters permitting import were subsequently issued. Approximately 82% 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 Jan 2016 to 31 Mar 2016



4.4 Process timings – Objection letters

A total of 69 Objections with Reason were issued in Q1/2016. Of these, 3 were issued where acknowledgements had previously been issued. These were a set of three identical notifications from a single importer submitted simultaneously, however only one letter was issued within 6 days of the acknowledgment. The importer was therefore aware of the objections to import of this Centrally Authorised product. The two outstanding letters were, however, issued beyond 28 days from acknowledgment for clarity and completeness.

4.4.1 Summary of reasons for objections to import

Table 7 Reasons for objection to import

Summary	Number of notifications
Centrally Authorised product available	41
Lack of assurance of GMP compliance	22
Importer's licence not valid for activity	5
Equivalent UK licensed product available	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.

To ensure imported unlicensed medicines comply with acceptable Good Manufacturing Practices the MHRA may request 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 the notified product or a similar product by a EU Member State or other PIC/S member. Evidence originating from non-PIC/S members will not be acceptable.

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.

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. Eight inspections were supported in Q1/2016 and a number of Inspectorate and Enforcement general queries answered.

6 Conclusions

The import notification system has operated substantially within the requirements of the regulations during Quarter 1, 2016.