Unlicensed Imports	May 2015

Summary Report for Importation of Unlicensed Medicines

01 Oct 2014 – 31 Dec 2014

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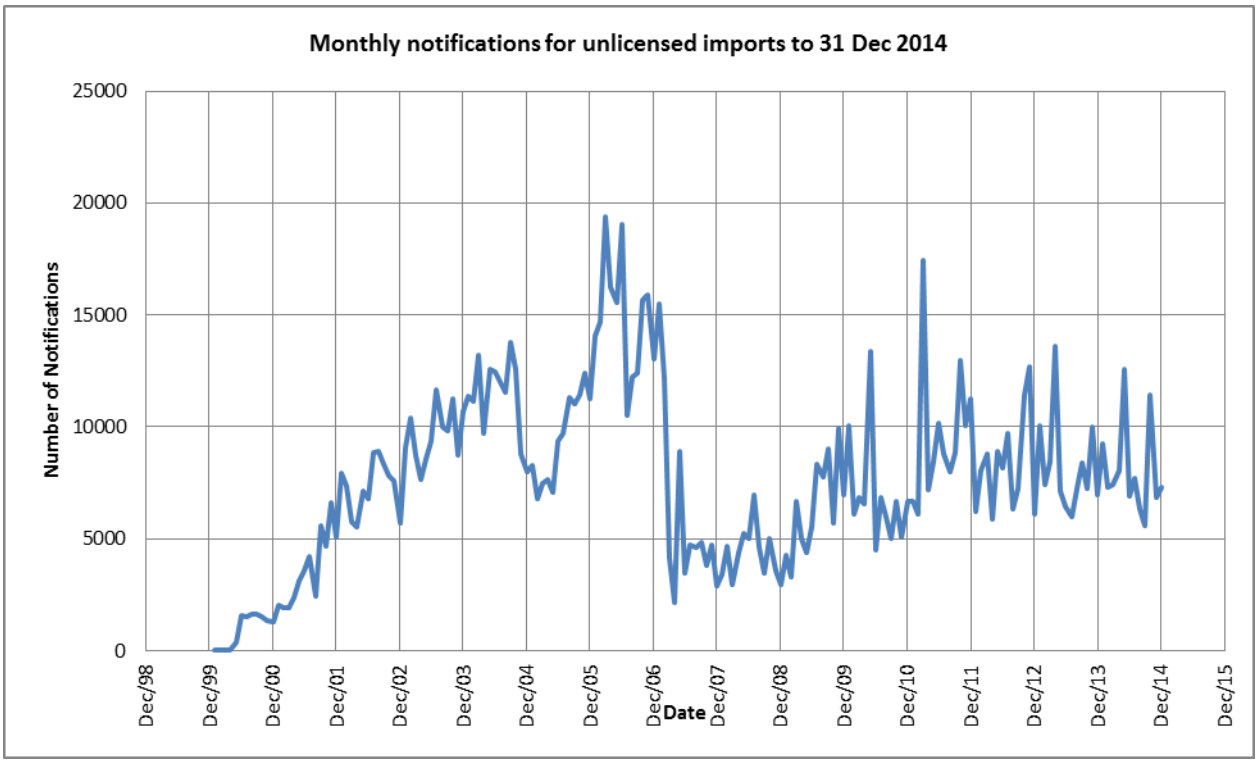
1 Introduction and Summary

The current report covers the period 01-October-2014 to 31-December-2014 and shows the import notification system to be operating substantially within the requirements of SI 2012/1916

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 Oct – 31 Dec 2014

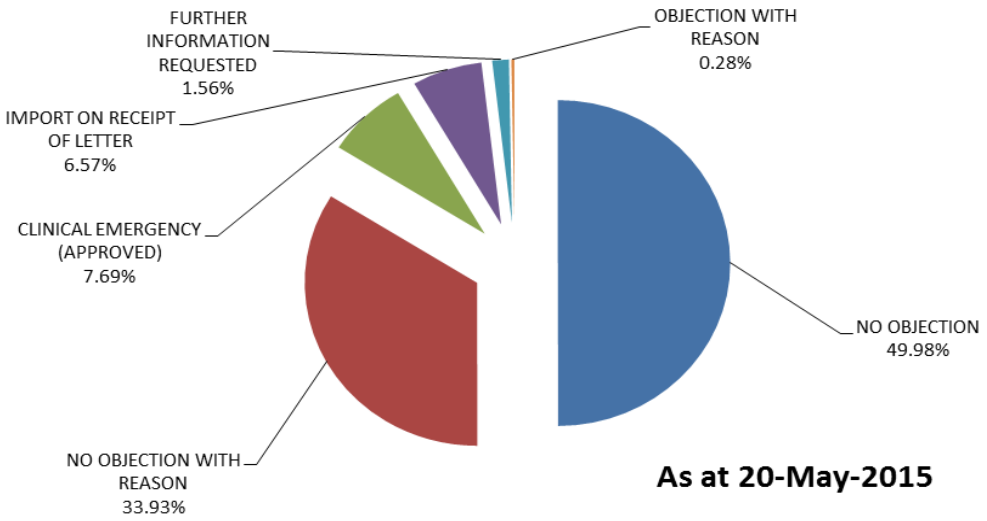


Table 1 Breakdown of valid notifications by importer, 01 Oct – 31 Dec 2014

Importers	Number of Notifications	Percentage Share
84 Importers	25328	100%
Of which 6 importers	19075	~75%

2.1 Countries of export of products

Table 2 Breakdown of valid notifications by country, 01 Oct – 31 Dec 2014

Rank	Exporting Country	Number of Notifications
1	United States of America	7527
2	Germany	6270
3	France	1609
4	India	1457
5	Spain	1329
6	Canada	1206
7	Italy	1282
8	Australia	1008
9	Austria	611
10	Switzerland	533
11	Belgium	414
12	Denmark	371
13	The Netherlands	333
14	Norway	299
15	Republic of Ireland	290
16	Czech Republic	233
17	Poland	148
18	Portugal	138
19	Japan	91
20	Greece	76
21	Hungary	28
22	Russia	20
23	Guernsey	15
24	Sweden	13
25	Finland	12
26	South Africa	8
27	New Zealand	5
28	Israel	2
	Sum:	**25328**
	EEA	**13471**
	Non-EEA	**11857**

2.2 Most frequently notified products

Table 3 lists the 50 most frequently notified products during Q4/2014 in rank order. The data are for valid notifications only and do not include cancellations or incomplete notifications. The listing includes notifications which may not be intended for placing on the UK market. It includes both acceptable products and those to which objections to import have been raised. It is therefore not an indicator of product acceptability.

Table 3. Top 50 Products by rank order of number of notifications received

Note: These rankings were obtained manually and although believed to be representative may contain errors

Rank	Product Name	Number of Notifications
1	Melatonin Oral Preps	3509
2	Midodrine Tablets All Strengths	2028
3	Carmustine Injection 100 mg	1200
4	Homoeopathics & Herbals	755
5	Vitamins - Oral Preps	728
6	Thyroid Oral Preps	719
7	Acetylcysteine Oral Preps	687
8	Co-Trimoxazole Parenterals	573
9	Ibrutinib 140 mg Capsules	460
10	Potassium Chloride SR Tablets/Caps	420
11	Bisacodyl Enemas 10 mg	413
12	Allergy Tests	341
13	Fosfomycin Oral Preps	310
14	Tretinoin/Vitamin A & Hydroquinone Topicals (Creams Oints., Gels Etc.)	306
15	Iloprost Injections & Infusions	251
16	Povidone-Iodine Ophthalmic Solns	250
17	Fluoxetine 10 & 20mg Oral Preps	249
18	Carfilzomib 60mg Inj	227
19	BCG Instillations	222
20	Sodium Nitroprusside 50mg Pow/Soln For Inj	221
21	Ketamine Injections	205
22	Fumaric Acid Ester Tablets All Strengths	196
23	Pentosan Polysulphate Sodium 50 & 100mg Capsules	190
24	Dasabuvir Tabs 250 mg	188

Rank	Product Name	Number of Notifications
25	Chloramphenicol Injections	186
26	Dexbrompheniramine & Psuedoephedrine 6 mg + 120 mg Tablets	180
27	Ombitasvir/Abt-450/Ritonavir Tabs	176
28	Vitamins - Parenteral Preps	170
29	Benzathine Penicillin Injections	169
30	Metolazone 2.5mg & 5mg Tablets	161
31	Progesterone Injections 100 mg/ml	161
32	Nitrofural 2 mg/g Ointment	160
33	[^{177}lutetium]-Dota^{0}-Tyr^{3}-Octreotate Parenteral	156
34	Lorazepam 4mg/ml Injections	148
35	Sodium Chloride 5% Eye Ointment	148
36	Talc For Pleurodesis	143
37	Pirenzepine 50mg Tablets	137
38	Sucralfate Oral Preps	133
39	Flunarizine 5 & 10 mg Tablets And Capsules	130
40	Insulin Injections	128
41	Betamethasone 4mg/ml Injections	127
42	Ribavirin 200 mg Tablets	120
43	Clindamycin 75 mg/5 ml Suspensions	119
44	SLIT & SCIT Allergy Treatments	115
45	Ticarcillin + Clavulanic Acid 3.1g Powder For IV Injection	114
46	Vasopressin 20 USP Units/ml Injections	114
47	Tiopronin 100 & 250 mg Tablets	111
48	Triamcinolone Topical Preps (Dental & Otic), Incl With Neomycin, Gramicidin, Nystatin	102
49	Demeclocycline Oral Preparations	100
50	Sultiame Tablets All Strengths	100

2.3 Vaccines

It should be noted that for vaccines, where any second administration is more than 3 months after the first, the maximum quantity permitted per notification is 25 unit doses.

Table 4 gives a summary of vaccine notifications for Q4/2014. As with the listings for other products, the data are for valid notifications only and do not include

cancellations or incomplete notifications. The listing includes notifications which may not be intended for placing on the UK market. It includes both acceptable products and those to which objections to import have been raised. It is therefore not an indicator of product acceptability.

Table 4 Vaccines/Immunoglobulins notified by rank order of number of notifications

Rank	Proprietary Name	Number of Notifications
1	BCG Instillations & Vaccines	222
2	Lymphocyte Immune Globulin Anti Thymocyte Globulin (Equine) 50 mg/ml Injection Soln	75
3	Measles + Rubella Vaccine 0.5ml Vials	32
4	Measles Vaccine 0.5ml	21
5	DTAP/IPV/HIB 0.5ml	14
6	Anti-Rho (D) Immune Globulin (Human) 1500iu	12
7	DTAP 0.5ml	9
8	Rabies Immune Globulin	7
9	Diphtheria + Tetanus + Pertussis + Poliomyelitis Vaccine 0.5 ml	6
10	Low Dose TDAP/IPV Tetanus, Diphtheria, Pertussis And Polio 0.5ml	5
11	Menjugate 0.5ml Vial 1x1	2
12	Tuberculin PPD	2
13	Anti-Human T-Lymphocyte Immunoglobulin 20mg/ml	1
14	Diphtheria, Tetanus, Acellular Pertussis,Hep B, IPV, HIB 0.5ml	1
15	Rabies Vaccine 2.5 IU/0.5ml	1

2.4 Shortages

Table 5. Products notified claiming UK product shortages, 01 Oct – 31 Dec 2014

Product Name	Number of Notifications
Co-Trimoxazole Injections	594
Potassium Chloride SR Tablets & Capsules	419
BCG Instillations & Vaccines	222
Ketamine Injections	203
Chloramphenicol Injections	171
Lorazepam Injection 4mg/ml	152
Progesterone Injection 100mg/ml	142
Sucralfate Oral Preps	132
Betametasone 4mg/ml Inj	116
Demeclocycline /150 & 300 mg Oral Preps	110
Vasopressin Injections & Infusions	109
Ticarcillin + Clavulanic Acid 3.1 Powder For Iv Injection 1x1	91
Iobitriodol 300mg Iodine Per ml	53
Trifluoperazine 1 & 5 mg Tabs	36
Potassium Chloride 0.4mmol/ml	28

Product Name	Number of Notifications
Acetylcysteine 200mg/ml Soln For Inj	25
Pyrimethamine 25mg Tablets	22
Levothyroxine Tablets Various Doses	21
Co-Phenotrope 2.5mg And 25mcg Tabs	20
Aciclovir Eye Ointment 3%	19
Infanrix/IPV/HIB 0.5ml PFS	18
Phentolamine Mesylate Injection 10mg/ml	16
Acetazolamide 250 mg Tablets	13
Perphenazine Tablets 2 & 4 mg	13
Edrophonium 10mg/ml Injection	12
Tetracosactide 0.25mg/ml Inj	10
Liothyronine Tablets Various Doses	9
Benzathine Benzylpenicillin 2.4MU Inj	8
Bumetanide 2mg/4ml Inj	8
Chlordiazepoxide 10mg Tablets	8
Diphenoxylate Hydrochloride + Atropine Sulfate 2.5 mg + 25 mcg Tablets	8
Cytarabine 2 G/20 ml Injections	7
Tetanus, Diphtheria, Pertussis And Polio Low Dose TDAP/IPV 0.5ml Pfs	7
Amsacrine 75 mg Injection	6
Potassium Canrenoate 250mg/10ml Injection	5
Promazine Hydrochloride 25 mg Tabs	3
Clavulanate Potassium; Ticarcillin Disodium 3.1g Injection	2
Ketotifen Tablets/1mg	2
Meptazinol Hydrochloride 100mg Injection	2
Cosyntropin Zinc Hydroxide Depot 1 mg/ml Injection Susp	1
Human Albumin Biotest Soln For Infus	1
Ibuprofen Lysine Sol For Inj	1
Isoprenaline Solution For Injection/0.2mg/ml	1
Vecuronium Bromide Inj 10mg	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 submitter, 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 Oct – 31 Dec 2014

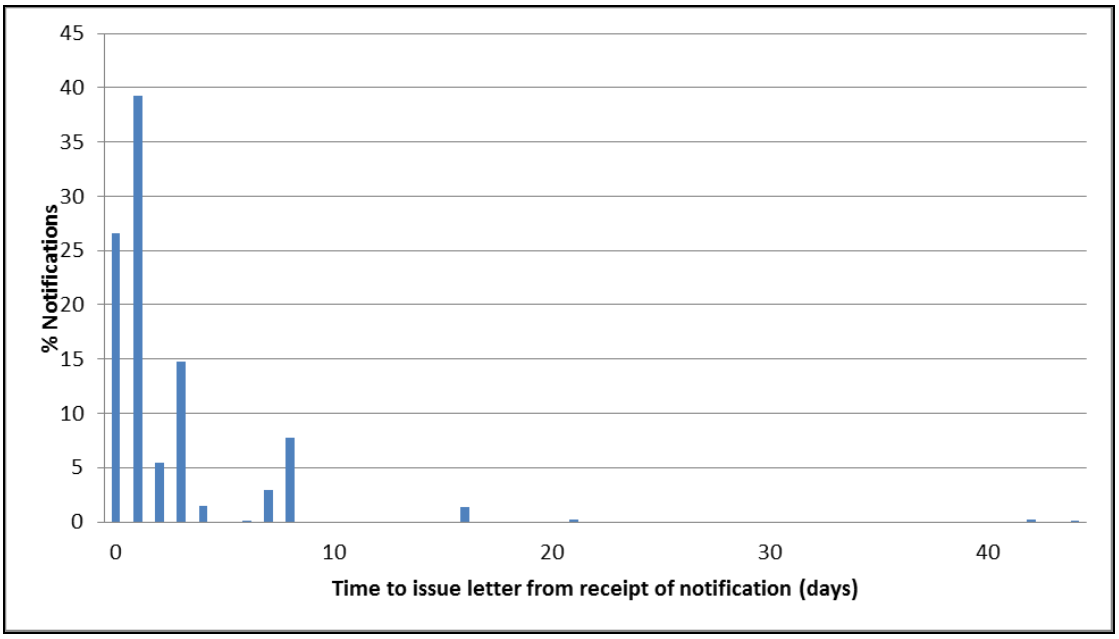


Table 6 Summary of Timings for Issuing Clinical Emergency Letters, 01 Oct – 31 Dec 2014

Time to Process from Receipt	Number of Notifications	% Notifications
% ≤ 4 days	1703	87.4
% ≤ 1 day	1282	65.8
Total Clinical Emergencies processed	1948	

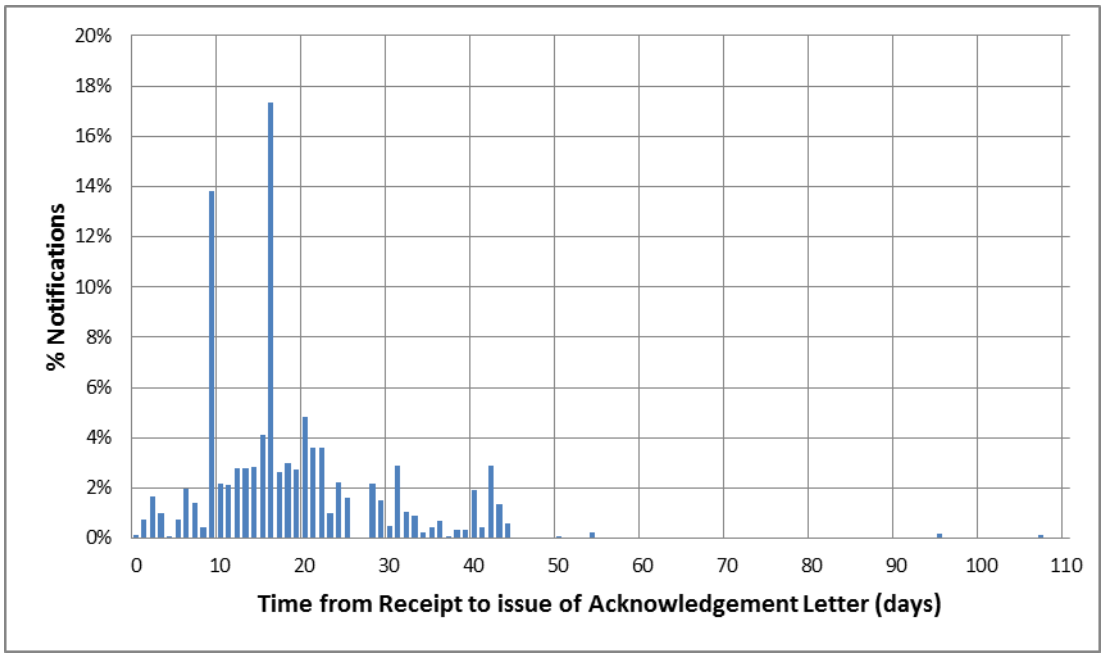
3.2 Process timings – Routine notifications

Graph 4 shows statistics for 12,174 notifications for Q4/2014 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 88% of acknowledgements were issued within 1 month of receipt of notifications.

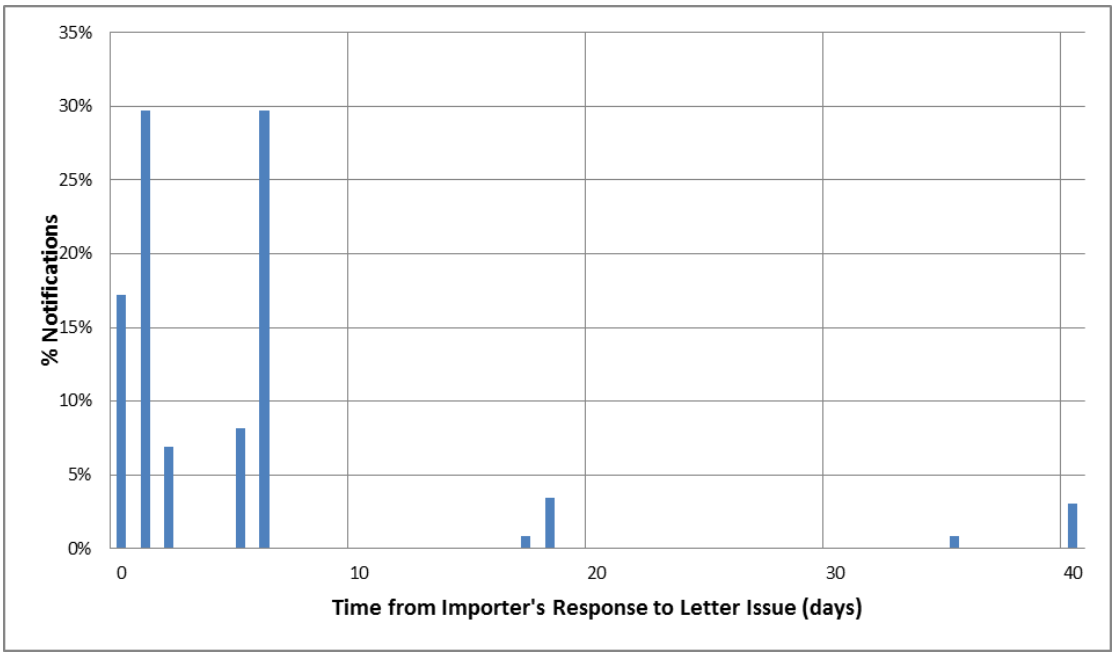
Graph 4 Time to issue Acknowledgements, 01 Oct – 31 Dec 2014



3.3 Process timings - Time to issue letters after receipt of further information request responses

Importers responded to 232 requests for further information from the MHRA in Q4/2014 and letters permitting import were subsequently issued. Approximately 92% of these final letters were issued within 6 days of receiving the importer's response. See Graph 5.

Graph 5 Response times to further information provided, 01 Oct – 31 Dec 2014



3.4 Process timings – Objection letters

A total of 70 Objections with Reason letters were issued in Q4/2014. Of these, 64 were issued where acknowledgements had previously been issued. 3 objections were issued on day 29, but not imported, 20 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

The most common reason for objections to import in Q4/2014 was submission of notifications for products with Centrally Authorised Marketing Authorisations (MAs) valid in all EU Member States. These are not unlicensed medicines and cannot be notified for import as such into the UK. The correct method of distribution is either by the MA holder or by way of authorised parallel distribution

There were also a number of notifications received where an equivalent nationally licensed product was available in the UK.

Some objections to import were raised due to known GMP concerns with specific manufacturers and with safety concerns where the European Medicines Agency's (EMA) Committee for Medicinal Products for Human use (CHMP) has said that oral medicines containing ketoconazole should no longer be used for the treatment of fungal infections.

Table 7 provides a summary of the objections raised in Q4/2014. Some notifications had more than one reason for objection to import.

Table 7 Reasons for objection to import

Summary	Number of notifications
Centrally Authorised product available	28
UK licensed product available	24
GMP concerns	18
Safety concerns (following CHMP opinion on ketoconazole)	11
Excessive quantity over that permitted in SI 2012/1916	3

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. Three inspections were supported in Q4/2014 and a number of Inspectorate general queries answered.

5 Conclusions

The Import Notification System is operating substantially within the requirements of SI 2012/1916.

Delays in printing urgent letters have been highlighted in staff training updates. The need for increased vigilance for notifications incorrectly made for importation of Centrally Authorised products as unlicensed medicines has also been highlighted.