Unlicensed Imports	Dec 2014

Summary Report for Importation of Unlicensed Medicines

01 Apr 2014 – 30 Jun 2014

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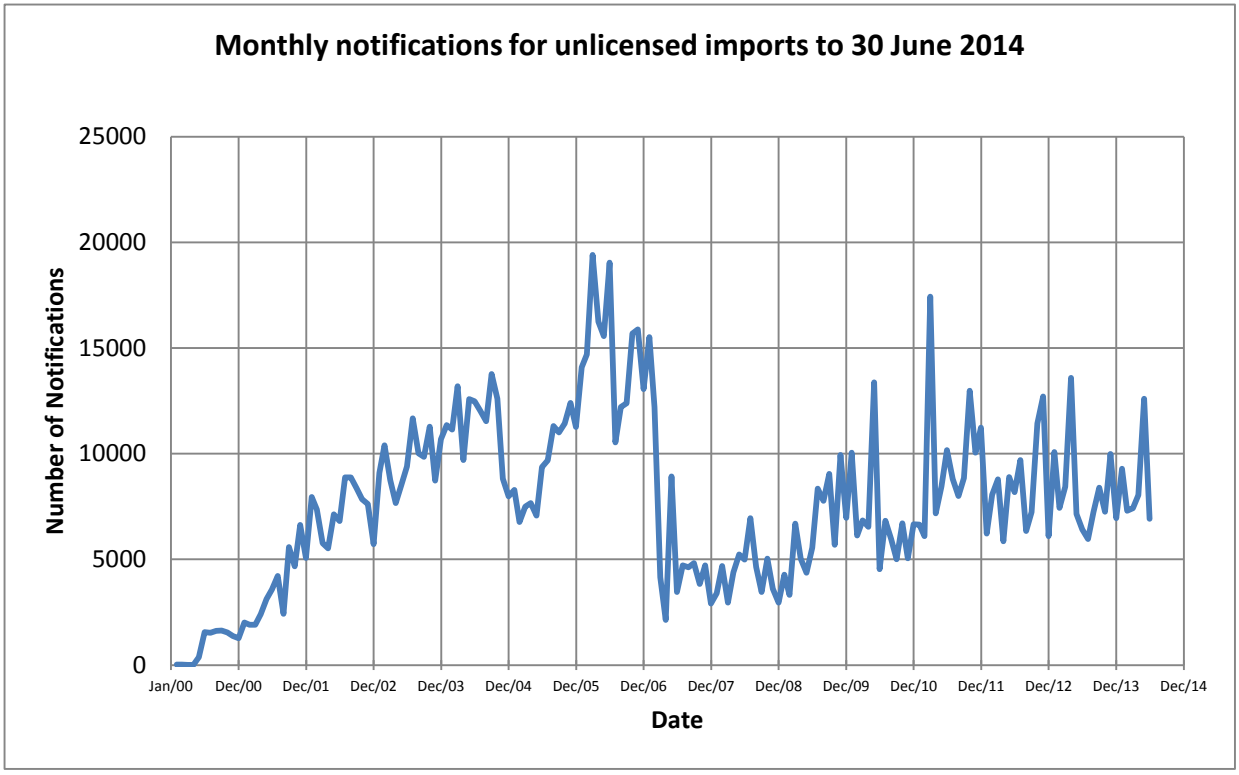
1 Introduction and Summary

The current report covers the period 01-April-2014 to 30-June-2014 and shows the import notification system to be operating substantially within the requirements of SI 2012/1916. It is hoped that the information provided will be found to be relevant and useful.

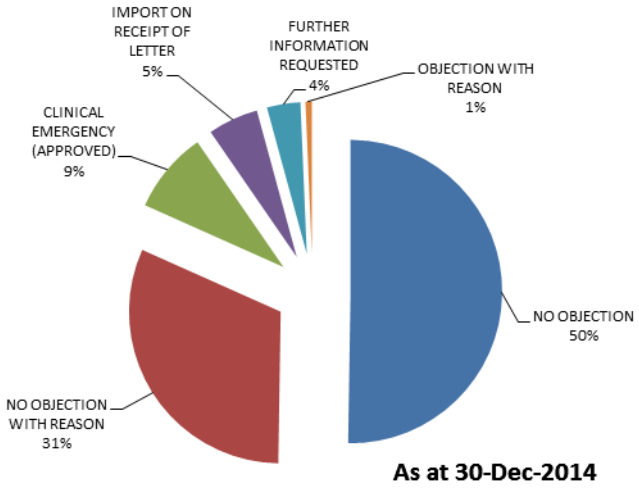
2 Notifications for importation

Graph 1 Monthly notifications for unlicensed imports

Note: Excludes invalid and cancelled notifications



Graph 2 Breakdown of notifications by status, 01 Apr – 30 Jun 2014



27,827 notifications were received from 81 importers for the period 01-Apr-2014 to 30-Jun-2014

2.1 Countries of export of products

Table 1 Breakdown of valid notifications by country, 01 Apr – 30 Jun 2014

Rank	Exporting Country	Approx. % Contribution
1	Germany	29.00
2	United States of America	13.49
3	India	10.35
4	France	7.82
5	Canada	6.72
6	Italy	6.34
7	Spain	5.59
8	Australia	3.08
9	Austria	2.57
10	Belgium	2.27
11	The Netherlands	2.10
12	Denmark	1.87
13	Switzerland	1.70
14	Republic of Ireland	1.60
15	Poland	1.26
16	Japan	1.03
17	Czech Republic	1.01
18	Hungary	0.50
19	New Zealand	0.46
20	Norway	0.39
21	Sweden	0.33
22	Greece	0.24
23	Slovakia	0.07
24	Portugal	0.06
25	Finland	0.05
26	South Africa	0.05
27	Brazil	0.03
28	Lithuania	0.01
	Sum:	**100.00**
	EEA	**63.10**
	Non-EEA	**36.90**

2.2 Most frequently notified products

Table 2 lists the 50 most frequently notified products during Q2/2014 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 2. 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	Midodrine Tablets All Strengths	2684
2	Co-Proxamol Oral Preps	2002
3	Ketamine Injections	1400
4	Homoeopathics & Herbals	740
5	Carmustine Injections	725
6	Vitamins - Oral Preps	725
7	Oral Thyroid Preparations	697
8	Acetylcysteine Oral Preps	565
9	Povidone-Iodine 5% Ophthalmic Soln	507
10	Allergy Diagnostic Tests	472
11	Sucralfate Oral Preps (Suspensions, Powders, Tablets)	424
12	Rifaximin 200 mg Tablets	375
13	Insulin, Human Injections	314
14	Melatonin Oral Preps	312
15	Sodium Nitroprusside Injections	294
16	Tetracosactrin Injections (Incl Depot)	282
17	Tretinoin/Vitamin A & Hydroquinone Topicals (Creams Oints., Gels etc.)	246
18	Clindamycin Suspensions & Granules	233
19	Fumaric Acid Ester Tablets all Strengths	228
20	Triamcinolone Injections	225
21	Lenvatinib Capsules	219
22	Fosfomycin Oral Preps	210
23	Mepivacaine 3% Injections	202
24	Talc for Pleurodesis	199
25	Progesterone Injections	191
26	Vitamin Injections	187
27	Metolazone 2.5 & 5 mg Tablets	186
28	Benzathine Penicillin Injections	180
29	Fluoxetine 10 mg Tabs	179
30	Povidone Iodine Ointments	179
31	Lidocaine Topical Preps	170
32	Aztreonam Injections	168
33	Pirenzepine 50 mg Tablets	167
34	Iloprost Injections	165
35	Mexiletin 100 & 200 mg Capsules	150
36	Reslizumab 100 mg Injections	141
37	Sultiame Tablets 50 & 200 mg Tablets	133
38	Sodium Chloride Parenterals	128
39	Paclitaxel 100 mg Injections	125
40	Patent Blue Injections	125

Rank	Product Name	Number of Notifications
41	Bisacodyl Enemas 10mg	124
42	Decitabine 50 mg Injections	124
43	Cardioplegia Solutions	121
44	Pentosan Polysulfate Capsules	121
45	Thyroid Injections	118
46	Clonazepam Injections	113
47	Diazoxide Oral Preps	111
48	Idebenone Tablets	111
49	Isoprenaline Injections	111
50	Amantadine Oral Preps	107

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 3 gives a summary of vaccine notifications for Q2/2014. 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 3 Vaccines/Immunoglobulins notified by rank order of number of notifications

Rank	Product Name	Number of Notifications
1	Yellow Fever Vaccine Live Attenuated	70
2	BCG Injections/Infusions/Instillations	37
3	Varicella-Zoster Virus Vaccine Live (Oka/Merck Strain)	21
4	Lymphocyte Immune Globulin Anti Thymocyte Globulin (Equine)50mg/ml Injection	14
5	Tuberculin PPD RT23 SSI 2tu/0.1ml Inj Soln	12
6	Varicella Zoster Immunoglobulin 125 IU/5 ml Infusion Soln	9
7	Diphtheria Toxoid Adsorbed 2 1.E Inj	8
8	Rabies Immunoglobulin	7
9	Typhoid Vaccines	5
10	Haemophilus Influenzae Type B 10 mcg Pow/Soln For Inj	4
11	Hepatitis B Immunoglobulin 50 IU/ml Infusion	4
12	Rotavirus Vaccine (Live, Oral Pentavalent Vaccine)	3
13	Tetanus Immunoglobulin 250 IU/ml Injection Soln	3
14	IgM Enriched Normal Human Immunoglobulin Solution For Infusion 5%	2
15	Meningococcal ACWY Vaccine	2
16	Anti Human-T-Lymphocyte Immunoglobulin Conc/Infn 100mg/5ml 1x10	1
17	Polio Vaccine Inactivated Injection	1

2.4 Shortages

Table 4. Products notified claiming UK product shortages, 01 Apr – 30 Jun 2014

Product Name	Number of Notifications
Ketamine Injections	542
Sucralfate Oral Preps	414
Cortrosyn/Tetracosactide Injections (Incl Depot)	281
Potassium Chloride Retard 600 mg Tablets & Capsules	78
Vasopressin 20 USP Units/ml Sol for Inj	66
Vecuronium Bromide 10mg Inj Ampoules	63
Hyoscine Hydrobromide Injections	52
Progesterone Injection 100mg/ml	52
Trifluoperazine Tablets	52
Liothyronine 0.1mg/5ml Powder And Sol for Inj	45
Amantadine Syrup/10mg/ml 1x500ml	44
Valsartan Tablets	42
Co-Trimoxazole 480mg/5ml Ampoules	37
Verapamil Hydrochloride 5mg/2ml Vials	37
Disulfiram 200 & 500mg Tablets 1x30	32
Isoprenaline 0.2mg/ml Ampoules	32
Oxytocin Injections	28
Cytarabine 2 G/20 ml Injection Soln	21
Dihydroergotamine Mesylate Amp 1mg/ml	20
BCG Injections/Infusions	17
Perphenazine 2 & 4 mg Tablets	15
Edrophonium Chloride 10 mg/ml Injection	14
Fluorescein Sodium 1mg Ophthalmic Strips	12
Lorazepam 2 mg/ml Injection Soln	12
Testosterone Implants & Injections 100 mg 1 X 1	12
Clomipramine Tablets All Strengths	11
Amantadine 100 mg Capsules	8
Diphtheria Toxoid Adsorbed 2 1.E Inj	8
DTAP/IPV/HIB Vaccines	8
Liothyronine 20 Mcg Tablets	7
Acetazolamide 250 mg Tablets	5
Diphenoxylate Hydrochloride + Atropine Sulfate 2.5 mg + 25 Mcg Tablets	5
Dinoprostone 1mg Vaginal Gel	4
Pindolol 5 mg Tablets	4
Ranitidine 25mg/ml Ampoules	4
Hyoscine 1.54 mg Transdermal Patches	3
Ritodrine Hydrochloride 50 mg/5 ml Injection	3
Meningococcal ACWY Vaccine	2
Colestyramine 4g Powder for Oral Suspension	2
Chorionic Gonadotrophin Pow and Solvent for Inj 5000iu	1
Fluorescein Sodium 10% Vials	1
Heparin Sodium 500000iu/100ml Eyedrops	1
Hydroxocobalamin Depot 1 mg-Amps for Inj	1
Hyoscyamine Sulphate 0.2 mg Depot Tablets	1
Methotrexat1g/10ml Infusion Conc	1
Neostigmine Bromide 15 mg Tablets	1
Perphenazine + Amitriptyline Hydrochloride 2 +25mg Tabs	1
Prednisolone Acetate 25mg Susp for Inj	1
Promazine Tabs 25mg 1 X 50	1
Cotrimoxazole 480mg/5ml Injections	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 if the notification is received on a Friday afternoon. Some notifications can take longer if there are queries or if a medical assessment is required. A number of notifications originally submitted as non-emergencies have been processed as emergencies resulting from changes in circumstances. These show as extended processing times. Some delays in final letter printing were identified and are being addressed in training updates.

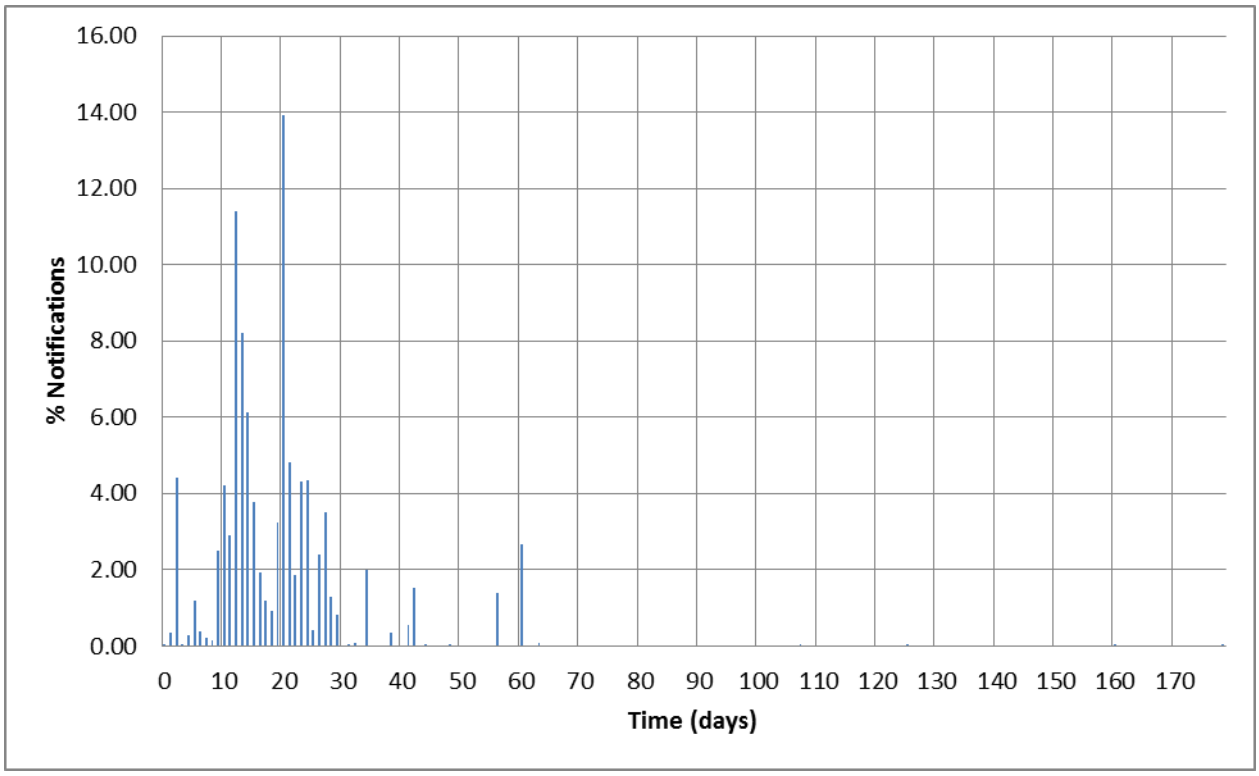
Table 5 Summary of Timings for Issuing Clinical Emergency Notifications, 01 Apr – 30 Jun 2014

	Number of Notifications	% Notifications
% ≤ 4 days	1490	62.76
% ≤ 1 day	1098	46.25
Total Clinical Emergencies processed	2374	

3.2 Process timings – Routine notifications

Graph 3 shows statistics for 4433 notifications for Q2/2014 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.

Graph 3 Time taken to issue Acknowledgement Letters after receipt, 01 Apr – 30 Jun 2014

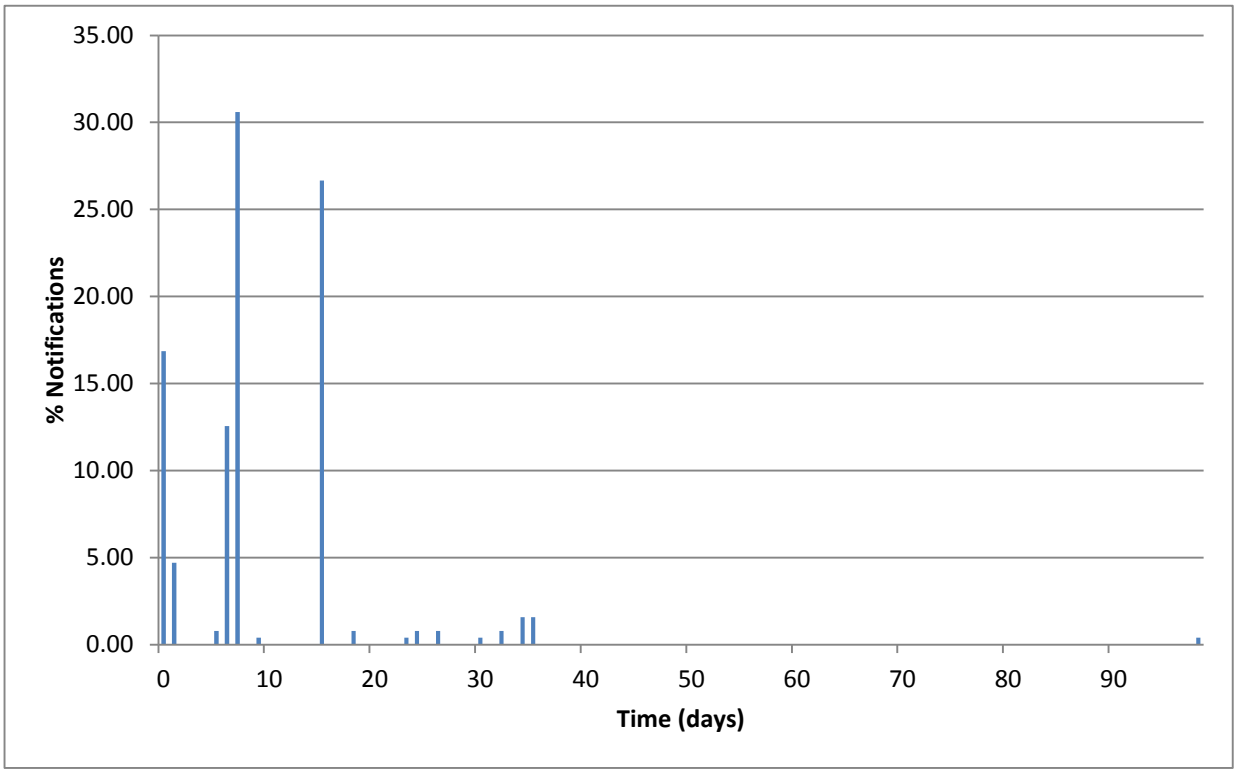


Approximately 90% of notifications were acknowledged within 28 days of receipt by the MHRA.

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.

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

Graph 4 Time to issue letters after receipt of further information request responses, 01 Apr – 30 Jun 2014



Importers responded to 255 requests for further information from the MHRA in Quarter 2 2014 and letters permitting import were subsequently issued. Approximately 90% of these final letters were issued within 2 weeks of receiving the importer's response. See Graph 4.

3.4 Process timings – Objection letters

121 Objection with Reason letters were issued where acknowledgements had previously been issued. 111 of these were issued within 28 days of the acknowledgement. The remaining letters, excepting 1, were issued in response to information provided by the importers following requests from the MHRA issued within 28 days of acknowledgments. Hence, these objection letters were issued in compliance with the regulations. The remaining single objection, issued at 126 days after acknowledgment, but assessed within 28 days of acknowledgment was for a

notification for import of a Centrally Authorised product, hence there were no safety concerns. There were 9 other identical objections, all of which were issued correctly within 28 days, hence the importer was in fact aware of the objection.

3.4.1 Summary of reasons for objection to import

The most common reasons for objection to import were incorrect or incomprehensible data in the notifications for import, frequently the use of the trade name in place of a generic name or INN, also failure to provide evidence of special clinical need where there may be an equivalent licensed product available in the UK is common.

Notifications were received for product manufactured by a company that was subject to a US FDA 483 letter citing potential GMP non-compliances.

It is becoming increasingly common for notifications to be received for import of Centrally Authorised products with Marketing Authorisations valid in all EU Member States. Objections are raised on the grounds of these not being unlicensed products. The correct method of distribution of these products is by way of parallel distribution. The MHRA does not, however, object where these products are intended for another Member State, but importers are advised to ensure they comply with applicable regulations in the receiving Member State.

There was a set of notifications from one importer where the importer had been asked to provide evidence of the manufacturer's compliance with European GMP or equivalent in the form of evidence of successful inspection of the manufacturing site by an EU Member State or other PIC/S member. The importer provided a GMP certificate issued by Brazil, which is not a PIC/S member.

Objections will be raised to importation where the quantities notified are not in compliance with the regulations.

There were 167 objections raised in Q2/2014.

Table 6 Summary of reasons for objection to import

Summary	Number of notifications
Missing data (Generic name/INN incorrect/not stated); No strength/dose	42
Similar licensed product available in the UK but no evidence of special clinical need for an unlicensed product was provided.	42
Manufacturer GMP non-compliance (these were all notifications from the same importer for the same product subject to a US FDA 483 letter)	40
Centrally Authorised and therefore not unlicensed products	33
No evidence of EU GMP compliance when requested	9
Excessive quantity not permitted under SI2012/1916	1

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. Twelve inspections were supported in Q2/2014 and a number of Inspectorate general queries answered.

5 Conclusions

The Import Notification System is operating substantially within the requirements of SI 2012/1916, although one potential non-compliance was found where an objection letter had been issued beyond the 28 day requirement, however there were no safety implications, and investigation showed that the importer was in fact already aware of the objection.

Delays in printing urgent letters have been highlighted in staff training updates.