



Summary Report for Importation of Unlicensed Medicines

01 Apr 2015 – 30 Jun 2015

| | | |
|----------|-----------------------|----------------------|
| Author | G. P. Matthews | Date: 03-Dec-2015 |
| Approved | S. Bax | Date: 03-Dec-2015 |

Contents

| | | |
|----------|---|-----------|
| 1 | Introduction and Summary | 3 |
| 2 | Notifications for importation | 4 |
| 2.1 | Importers | 5 |
| 2.2 | Countries of export of products | 6 |
| 2.3 | Most frequently notified products | 7 |
| 2.4 | Vaccines and immunoglobulins | 8 |
| 2.5 | Shortages | 8 |
| 3 | Administrative matters | 10 |
| 3.1 | Process timings – Clinical Emergencies | 10 |
| 3.2 | Process timings – Routine notifications | 11 |
| 3.3 | Process timings - Further information request responses | 12 |
| 3.4 | Process timings – Objection letters | 12 |
| 4 | Inspection liaison | 14 |
| 5 | Conclusions | 15 |

1 Introduction and Summary

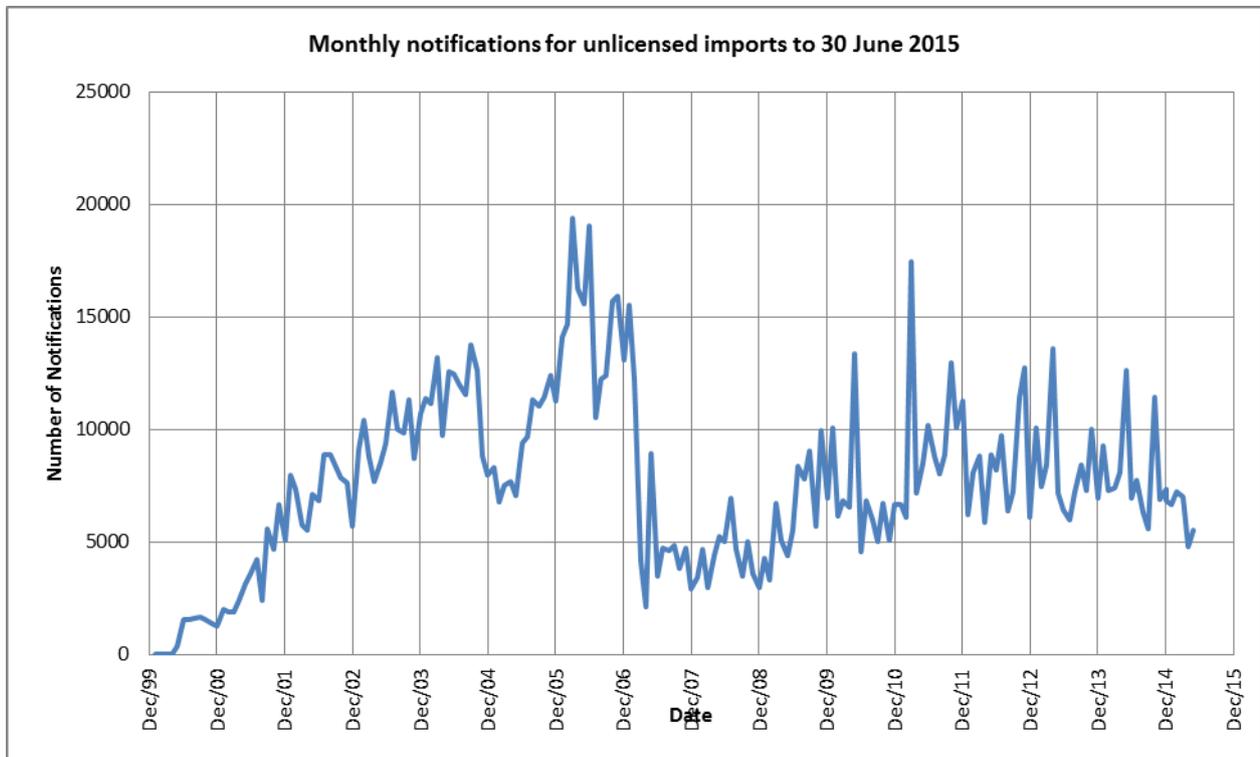
This report¹ covers the period 01-April-2015 to 30-June-2015 and shows the import notification system to be operating substantially within the requirements of SI 2012/1916.

¹ The data for this report were compiled on 29-Sep-2015 and reflect the Import Notification System at this date.

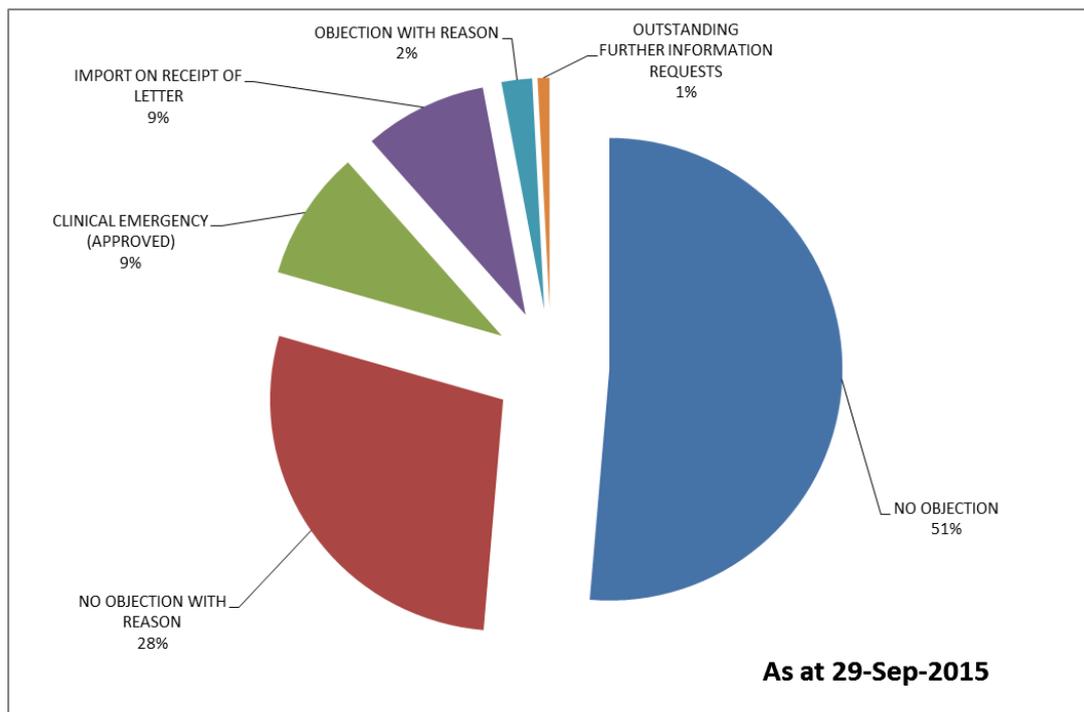
2 Notifications for importation

Graph 1 Monthly notifications for unlicensed imports

Note: Excludes invalid and cancelled notifications



Graph 2 Breakdown of valid notifications by status, 01 Apr – 30 Jun 2015



2.1 Importers

A total of 16992 notifications were received from 90 importers for the period 01 Apr 2015 to 30 Jun 2015. Of these, 6 importers accounted for approximately 74%.

Table 1 Valid notifications by importer 01 Apr 2015 to 30 Jun 2015

| Importer Details | Number of Notifications | Percentage Share |
|-------------------------|--------------------------------|-------------------------|
| 90 Importers | 16992 | 100.00% |
| Of which 6 importers | 12613 | ~74% |

2.2 Countries of export of products

Table 2 Countries of export 01 Apr 2015 to 30 Jun 2015

| Rank | Exporting Country | Number of Notifications | %Share |
|------|--------------------------|-------------------------|----------------|
| 1 | Germany | 4260 | 25.07% |
| 2 | United States of America | 3251 | 19.13% |
| 3 | Italy | 1549 | 9.12% |
| 4 | France | 1124 | 6.61% |
| 5 | Australia | 1095 | 6.44% |
| 6 | Spain | 1045 | 6.15% |
| 7 | Canada | 654 | 3.85% |
| 8 | Austria | 515 | 3.03% |
| 9 | Switzerland | 503 | 2.96% |
| 10 | The Netherlands | 472 | 2.78% |
| 11 | Belgium | 397 | 2.34% |
| 12 | India | 354 | 2.08% |
| 13 | Czech Republic | 326 | 1.92% |
| 14 | Denmark | 227 | 1.34% |
| 15 | Republic of Ireland | 209 | 1.23% |
| 16 | Poland | 198 | 1.17% |
| 17 | Japan | 164 | 0.97% |
| 18 | Portugal | 112 | 0.66% |
| 19 | Greece | 103 | 0.61% |
| 20 | Hungary | 99 | 0.58% |
| 21 | Norway | 85 | 0.50% |
| 22 | Argentina | 80 | 0.47% |
| 23 | Sweden | 50 | 0.29% |
| 24 | Finland | 37 | 0.22% |
| 25 | New Zealand | 20 | 0.12% |
| 26 | Slovakia | 11 | 0.06% |
| 27 | Guernsey | 10 | 0.06% |
| 28 | United Kingdom* | 8 | 0.05% |
| 29 | Romania | 8 | 0.05% |
| 30 | Estonia | 5 | 0.03% |
| 31 | Israel | 5 | 0.03% |
| 32 | Cyprus | 4 | 0.02% |
| 33 | South Africa | 3 | 0.02% |
| 34 | Turkey | 3 | 0.02% |
| 35 | Bulgaria | 2 | 0.01% |
| 36 | Puerto Rico | 2 | 0.01% |
| 37 | Lithuania | 1 | 0.01% |
| 38 | Russia | 1 | 0.01% |
| | Sum: | 16992 | 100.00% |
| | EEA | 10857 | 63.89% |
| | Non-EEA | 6135 | 36.11% |

*UK is not an acceptable country of import!

2.3 Most frequently notified products

Table 3 Top 50 frequently notified products 01 Apr 2015 to 30 Jun 2015

| Rank | Product Name | Number of Notifications | % all Notns |
|------|--|-------------------------|-------------|
| 1 | Melatonin Oral Preps | 1074 | 6.32% |
| 2 | Homoeopathics & Herbals | 766 | 4.51% |
| 3 | Thyroid Oral Preps | 619 | 3.64% |
| 4 | Povidone-Iodine Topical Preps | 494 | 2.91% |
| 5 | Acetylcysteine Oral Preps | 432 | 2.54% |
| 6 | Potassium Chloride Controlled Release Tabs & Caps | 410 | 2.41% |
| 7 | Benzathine Benzylpenicillin Injections | 407 | 2.40% |
| 8 | Vitamins - Oral Preps | 348 | 2.05% |
| 9 | Midodrine 2.5 & 5 mg Tablets | 341 | 2.01% |
| 10 | BCG Injections, Instillations, Infusions | 336 | 1.98% |
| 11 | Fosfomycin Oral Preps | 289 | 1.70% |
| 12 | Sucralfate Oral Preps | 258 | 1.52% |
| 13 | Tretinoin/Vitamin A & Hydroquinone Topicals (Creams Oints., Gels Etc.) | 254 | 1.49% |
| 14 | Allergy Tests | 246 | 1.45% |
| 15 | Pirenzepine 50mg Tablets | 246 | 1.45% |
| 16 | Fumaric Acid Esters 30 &120mg Tablets | 241 | 1.42% |
| 17 | Metolazone 2.5 & 5 mg Tablets | 212 | 1.25% |
| 18 | Indigo Carmine Injections | 196 | 1.15% |
| 19 | Furosemide Injections/Infusions | 177 | 1.04% |
| 20 | Bisacodyl Enemas | 176 | 1.04% |
| 21 | Iloprost 50 & 100 mcg Conc For Soln For Inj/Inf | 174 | 1.02% |
| 22 | Sodium Nitroprusside 50mg Inj/Inf | 152 | 0.89% |
| 23 | Clindamycin Oral Suspensions | 149 | 0.88% |
| 24 | Sodium Chloride 5% Eye Ointment | 141 | 0.83% |
| 25 | Talc For Pleurodesis | 136 | 0.80% |
| 26 | Flunarizine Tablets & Capsules All Strengths | 134 | 0.79% |
| 27 | Procaine Benzylpenicillin Injections | 131 | 0.77% |
| 28 | Lu-Dota, Tyr Ocfreotate, Lutetium-177 (177Lu) Labelled | 130 | 0.77% |
| 29 | Mercaptopurine Tablets All Strengths | 126 | 0.74% |
| 30 | Mexiletene Capsules All Doses | 123 | 0.72% |
| 31 | Progesterone Creams | 122 | 0.72% |
| 32 | Paracetamol 250 & 500mg Granules | 121 | 0.71% |
| 33 | Ibuprofen 75mg & 150mg Suppositories | 120 | 0.71% |
| 34 | Paracetamol 1000mg & 75mg Suppositories | 120 | 0.71% |
| 35 | Paracetamol and Codeine 500mg/30mg & 1000mg/60mg Suppositories | 120 | 0.71% |
| 36 | Carfilzomib 60 mg Lyophilized Injections | 118 | 0.69% |
| 37 | Diazoxide 50mg/ml Oral Suspensions | 118 | 0.69% |
| 38 | Ornithine Aspartate Granules/Oral Sol 3&5g | 117 | 0.69% |
| 39 | Melphalan 50 mg Injections | 111 | 0.65% |
| 40 | Ciclosporin Ophthalmic Preps | 110 | 0.65% |
| 41 | Isoniazid Oral Preparations | 97 | 0.57% |
| 42 | Pentosan 50 & 100 mg Capsules | 96 | 0.56% |
| 43 | Demeclocycline Tabs & Caps | 95 | 0.56% |
| 44 | Insulin Preps | 95 | 0.56% |
| 45 | Cotrimoxazole Infusions | 90 | 0.53% |
| 46 | Progesterone Injections (Incl Depot) | 82 | 0.48% |
| 47 | Saline In Glass 0.90% | 80 | 0.47% |
| 48 | Carmustine 100 mg Pow/Soln For Inj | 76 | 0.45% |
| 49 | Cyproheptadine Liquid/2mg Per 5ml | 76 | 0.45% |

| Rank | Product Name | Number of Notifications | % all Notns |
|------|--|-------------------------|-------------|
| 50 | Diphenoxylate Hydrochloride + Atropine Sulfate 2.5 mg + 25 mcg Tablets | 76 | 0.45% |

2.4 Vaccines and immunoglobulins

Table 4 Vaccines & immunoglobulins 01 Apr 2015 to 30 Jun 2015

| Rank | Non-Proprietary Product Name | Number of Notifications |
|------|---|-------------------------|
| 1 | BCG Instillations and Vaccines | 336 |
| 2 | TDAP | 19 |
| 3 | Antithymocyte Immunoglobulin | 18 |
| 4 | Meningitis B | 12 |
| 5 | Diphtheria + Tetanus + Pertussis + Polio + Hepatitis B + Haemophilus Influenzae | 8 |
| 6 | DTAP | 8 |
| 7 | DTAP/IPV/HIB | 8 |
| 8 | Hepatitis B (R-DNA) Vaccine (Adjuvanted, Adsorbed) | 8 |
| 9 | Tetanus, Diphtheria, Pertussis and Polio | 8 |
| 10 | Tuberculin PPD | 7 |
| 11 | Haemophilus Influenzae Type B | 5 |
| 12 | <i>Coxiella Burnetii</i> Purified Killed Suspension | 4 |
| 13 | Anti-D Immunoglobulin | 1 |
| 14 | CMV Immunoglobulin | 1 |
| 15 | Rabies Immune Globulin Human | 1 |
| 16 | Tetanus Immunoglobulin | 1 |

2.5 Shortages

Table 5. Products notified claiming UK product shortages, 01 Apr 2015 to 30 Jun 2015

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

| Proprietary Name | Number of Notifications |
|--|-------------------------|
| Potassium Chloride 600mg SR Tablets | 410 |
| BCG Instillations & Vaccines | 336 |
| Sucralfate Oral Preparations | 254 |
| Demeclocycline Tabs & Caps | 87 |
| Co-Trimoxazole Infusions | 77 |
| Co-Phenotrope 2.5 mg + 25 mcg Tablets | 75 |
| Etoposide 100mg/5ml Conc For Infusion Solution | 62 |
| Progesterone Injection 100mg/ml | 54 |
| Etoposide Capsules 50mg | 42 |
| Iobitriodol 300mg Iodine Per ml | 30 |
| Methotrexate Injections | 17 |
| Dexamethsone 4 mg Tablets | 16 |

| Proprietary Name | Number of Notifications |
|---|-------------------------|
| Ketamine Injections | 16 |
| Perphenazine 2 & 4mg Tablets | 15 |
| Disulfiram 500 mg Tablets | 12 |
| Phenoxybenzamine Capsules 10mg | 12 |
| Benzathine Benzylpenicillin Injections | 10 |
| DTAP/IPV/HIB 0.5ml Pfs | 8 |
| Low Dose TDAP/IPV 0.5ml pfs | 8 |
| Tuberculin 5iu/0.1ml Injection Soln | 7 |
| Liothyronine Tablets | 6 |
| Norfloxacin Tablets 400mg | 6 |
| Aspirin 300 & 600mg Suppositories | 5 |
| Povidone Iodine 5% Ophthalmic Solution | 5 |
| Gonadorelin 0.1mg/ml Injection Soln | 4 |
| Trifluoperazine Tabs & Caps | 4 |
| Bupivacaine & Adrenaline 0.25%W/V 1:200000inj | 4 |
| Chloramphenicol Sodium Succinate1 g Powder For Inj1 | 3 |
| Periactine Tablets 4mg | 3 |
| Tetracosactrin Hexa-Acetate 250 mcg/ml Injection Soln | 3 |
| Acetazolamide 250 mg Scored Tablets | 2 |
| Edrophonium Chloride 10mg/ml Injection | 2 |
| Human Albumin Sol For Infus 5% | 2 |
| Phentolamine Mesylate Injections 10mg/ml | 2 |
| Pyrimethamine 25mg Tablets | 2 |
| Amikacin 500 mg/2ml Injection Soln | 1 |
| Amino Acid Solution For Infusion | 1 |
| Digoxin 0.25 mg/ml Injection Soln | 1 |
| Oxytocin 10 lu/ml Inj/Inf Soln | 1 |
| Plerixafor Sterile Sol For Inj 20mg/ml | 1 |
| Triamcinalone Acetonide 10mg/L Inj Susp | 1 |
| Vasopressin 20units/ml Inj Soln | 1 |

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 Apr 2015 to 30 Jun 2015

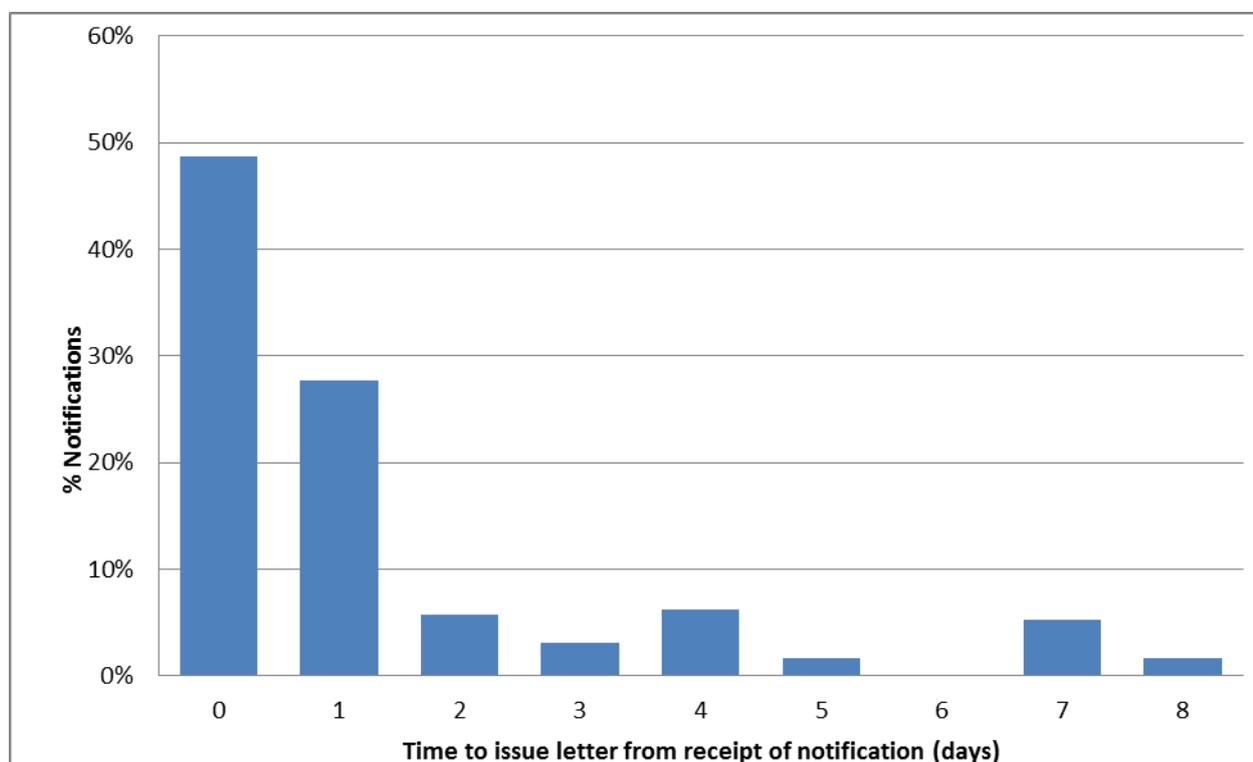


Table 6 Summary of Timings Clinical Emergency Letter Timings, 01 Apr 2015 to 30 Jun 2015

| Time to Process from Receipt | Number of Notifications | % Notifications |
|---|-------------------------|-----------------|
| % ≤ 4 days | 1407 | 91.36% |
| % ≤ 1 day | 1176 | 76.36 |
| Total Clinical Emergencies processed | 1540 | 100% |

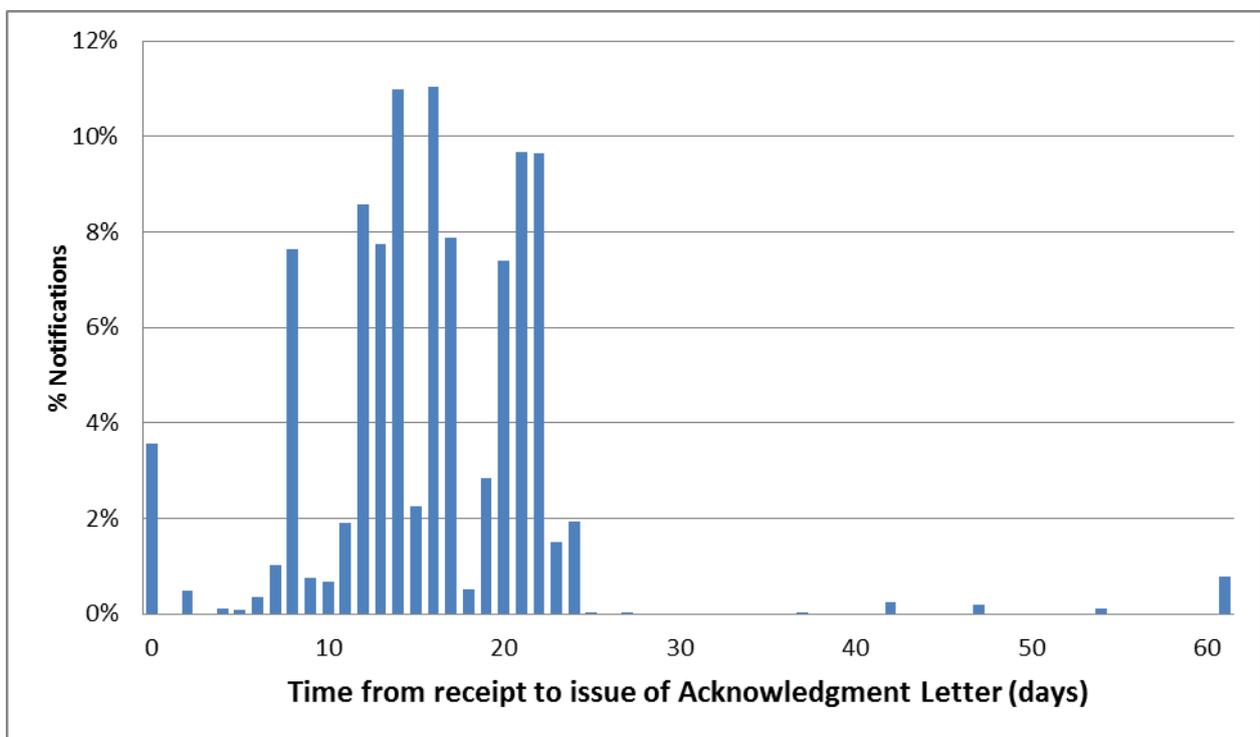
3.2 Process timings – Routine notifications

Graph 4 shows statistics for 2530 notifications for Q2/2015 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 22 days of receipt of notifications.

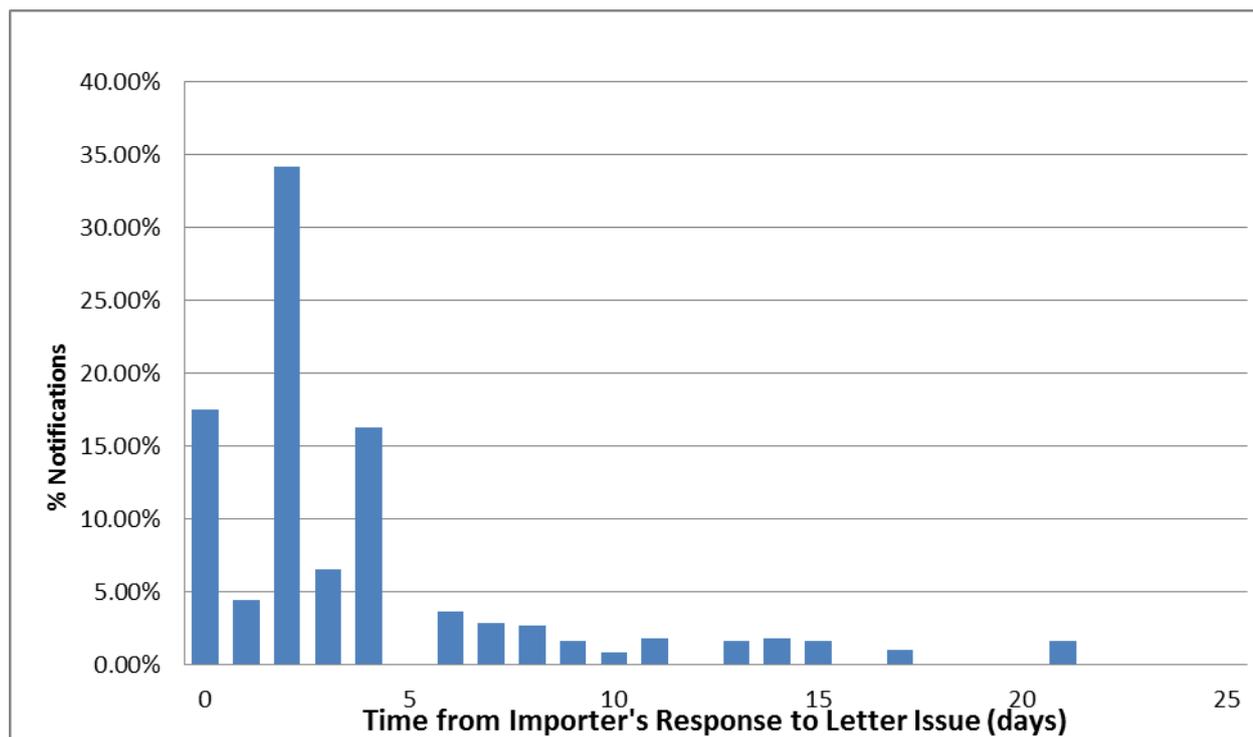
Graph 4 Time to issue Acknowledgements, 01 Apr 2015 to 30 Jun 2015



3.3 Process timings - Further information request responses

Importers responded to 492 requests for further information from the MHRA in Q2/2015 where letters permitting import were subsequently issued. Approximately 95% 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 Apr 2015 to 31 Jun 2015



3.4 Process timings – Objection letters

A total of 358 Objections with Reason letters were issued in Q2/2015. Of these, 3 were issued where acknowledgements had previously been issued. Each of these letters was issued within 28 days of acknowledgement.

3.4.1 Summary of reasons for objections to import

Table 7 Reasons for objection to import

| Summary | Number of notifications |
|--|-------------------------|
| UK licensed product available | 336 |
| GMP concerns | 8 |
| Excessive quantity over that permitted in SI 2012/1916 | 7 |
| Centrally Authorised product available | 6 |
| Importer's licence not valid for activity | 1 |

Following the launch in the UK of licensed midodrine and fosfomycin products, the most common reason for objecting to import in Q2 2015 was that there were equivalent UK licensed versions of these products available. Importers should ensure that they are aware of new product introductions and must cease supply of any equivalent unlicensed medicine unless there is a clinical reason why the licensed product cannot meet individual patients' clinical needs.

We continue to receive notifications for import of Centrally Authorised products. These 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.

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. Eight inspections were supported in Q2/2015 and a number of Inspectorate and Enforcement general queries answered.

5 Conclusions

The import notification system has operated substantially within the requirements of the regulations during Quarter 2, 2015.

The most significant issue encountered this quarter was the continuing supply of unlicensed medicines after launch of new licensed products.