EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Compliance & Inspections Department

Results of the sampling and testing programme for the year 2012

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Executive summary

This report concerns the 2012 sampling and testing programme coordinated by the European Medicines Agency in accordance with Regulation (EC) 726/2004, art. 57(r). A total of 41 products were sampled and tested, which required the cooperation of 35 inspectorates (for the sampling) and of 34 official laboratories (for the testing). Most of the products tested (97%) complied with the authorised specifications. One veterinary product was found to be out of specification, and an investigation took place in order to address this suspected quality defect.

Some checks on the printed packaging materials of the samples taken were also carried out. The purpose of these checks is to verify the compliance of the main information of the label and of the package leaflet (PL), with the authorised texts.

The sampling and testing programmes

Legal basis

Regulation (EC) No.726/2004, art. 57(r) – The Agency shall provide the Member States and the institutions of the European Union with the best possible scientific advice on any question relating to the evaluation of the quality, safety and efficacy of medicinal products for human or veterinary use which is referred to it in accordance with the provisions of EU legislation relating to medicinal products.

To this end, the Agency, acting particularly through its committees, shall undertake the following task: coordinate the supervision of the quality of medicinal products placed on the market by requesting testing of compliance with their authorised specifications by an Official Medicines Control Laboratory or by a laboratory that a Member State has designated for that purpose.

Scope of the programmes

The main aim of the programmes is to verify that the centrally authorised medicinal products on the market comply with their authorised quality specifications. Additionally, this monitoring activity allows verification that the analytical methods used by the manufacturers for the control of the products are satisfactory.

Partners

The success of the programmes is based on the cooperation and partnership of the following:

- European Medicines Agency (EMA) - overall management.
- European Directorate for the Quality of Medicines and HealthCare (EDQM) - coordination of the reporting and the sampling and testing.
- Network of Official Medicines Control Laboratories (OMCLs) in the EEA – testing.
- Inspection services of the EEA national competent authorities - sampling from the market.
- EMA scientific committees (CHMP and CVMP) - adoption of the programmes.
- Products' rapporteurs and co-rapporteurs - advice on testing recommendations and follow-up actions.

Report on the 2012 programme

Preparatory work

Lists of products to be tested were prepared by the EMA Compliance and Inspection Sector on the basis of a risk-based approach[1]. The lists were submitted to the CHMP and the CVMP in February 2011, and were adopted by the relevant committee. For the list of the products tested, see Annex 2.

Once the lists were endorsed and finalised, the Manufacturing and Quality Compliance Section wrote to the marketing authorisation holders (MAHs) of the selected products. They were informed of the inclusion of their products in the testing programme, and asked to provide the documentation and the material needed to carry out the testing.

Advice on the parameters to be tested for each product was obtained from the relevant rapporteurs.

Sampling

Samples of the products[2] were drawn by inspectors of the competent national authorities, from their respective national markets. When possible, each product was sampled in three different Member States.

Below is a table summarising the sampling phase.

Number of products	Number of inspectorates	Number of samples taken	Number of samples taken from the parallel distribution market
41	35	124	0

Label check and PL check

Label and PL checks were carried out by the samplers. A checklist was provided to the samplers to assist in this process.

The purpose of the exercise was not to perform a full label and PL check of compliance, but rather to highlight potential issues for further investigation. There were no reports of suspected non-compliances.

Testing

Testing of the products started in March 2012. Chemical products and insulin products were tested in one laboratory only. When needed, a back-up laboratory was available. Biological and veterinary immunological products were tested in two laboratories.

Below is a table summarising the testing phase.

Number of products tested	Number of Laboratories
41	34

[1] Development of risk based approach for the selection of products (EMEA/INS/S&T/120857/2008)

[2] For the purpose of the figures contained in this report, a 'product' can include 2 or more medicinal products (with different marketing authorisation numbers) which are identical. See also list in Annex 2.

Reporting

The EDQM prepared and sent CAP testing reports (one for each product) containing details of the testing results to the Agency on an on-going basis. Results were classified in a 1 – 3 scale, according to the testing outcome.

Below is a table summarising the results.

Products tested	1= No problems identified	2 = Issues identified	3 = Out of specification
Human = 33	17	16	0
Veterinary = 8	3	4	1
Total = 41	20	20	1

Report circulation

The testing reports were first circulated to the respective marketing authorisation holder (MAH), with the request to provide their comments.

The comments from the MAHs, and the reports, were then circulated to the rapporteurs with the request to provide advice for follow-up.

Outcome

Most of the problems identified during the testing were in relation to the detail of the analytical procedures authorised or used for the control of the medicinal products. In order to address these issues, the Manufacturing and Quality Compliance Section had extensive contacts with the MAHs, which resulted in most cases, in the MAH submitting a variation application and amending SOPs.

For the product reported to be `out of specification', a suspected quality defect procedure was initiated.

The MAH provided an explanation and the risk assessment evaluated by the rapporteurs led to a submission of a variation to modify one of the specifications.

Conclusion

The results of the 2012 programme showed that most of the products tested were in compliance with the authorised specifications, with one veterinary product found to be outside its specifications. A quality defect procedure was initiated and an investigation was carried out. As a result the MAH will submit a variation to modify one of the product specifications.

For about 48% of the marketed products tested (20 out of 41) some issues of technical, scientific, regulatory or editorial nature were identified, and these were addressed in co-operation with the MAH and the rapporteurs.

In view of the results obtained in the 2012 sampling and testing programme, it can be concluded that this annual monitoring exercise continues to be an important tool in the implementation of the Agency's task of supervision of medicinal products placed on the market.

Annex 1: Acronyms

CAP:	Centrally authorised product
CHMP:	Committee for Medicinal Products for Human Use
CVMP:	Committee for Medicinal Products for Veterinary Use
EDQM:	European Directorate for the Quality of Medicines and HealthCare
EEA:	European Economic Area, formed by the Members of the European Union and Iceland, Liechtenstein and Norway
MAH:	Marketing authorisation holder
OMCL:	Official Medicines Control Laboratory
PL:	Package leaflet

Annex 2: List of products tested in the 2012 programme

	Product	**Pharmaceutical form**	**Human/ Veterinary**
1	Advagraf	Prolonged-release hard capsule	Hum
2	Alimta	Powder for concentrate for solution for infusion	Hum
3	BTVPUR Alsap 8	Suspension for injection	Vet
4	Byetta	Solution for injection	Hum
5	Cellcept	Capsule, hard	Hum
6	Cellcept	Film-coated tablet	Hum
7	Cellcept	Powder for oral suspension	Hum
8	Cellcept	Powder for concentrate for solution for infusion	Hum
9	Cimzia	Solution for injection	Hum
10	CoAprovel,	Tablet	Hum
11	CoAprovel	Film-coated tablet	Hum
12	Controloc Control	Gastro-resistant tablet	Hum
13	Docetaxel Teva	Concentrate and solvent for solution for infusion	Hum
14	Eucreas/Zomarist/Icandra	Film-coated tablet	Hum
15	Fareston	Tablet	Hum
16	Halocur	Oral solution	Vet
17	Herceptin	Powder for concentrate for solution for infusion	Hum
18	Irbesartan/ Hydrochlorothiazide	Film-coated tablet	Hum
19	Kuvan	Soluble tablet	Hum
20	Leucogen	Suspension for injection (imm)	Vet
21	MabCampath	Concentrate for solution for infusion	Hum
22	Mepact	Powder for suspension for infusion	Hum
23	Metacam	Solution for injection	Vet
24	Metacam	Oral suspension	Vet
25	Metacam	Chewable tablets	Vet
26	Myclausen	Film-coated tablet	Hum
27	Neocolipor	Suspension for injection (imm)	Vet
28	Neupro	Transdermal patch	Hum
29	Omnitrope	Solution for injection in a cartridge	Hum
30	Pegasys	Solution for injection	Hum
31	Porcilis AR-T DF	Suspension for injection (imm)	Vet
32	Ratiograstim	Solution for injection for infusion	Hum
33	Removab	Concentrate for solution for infusion	Hum
34	Rilutek	Film-coated tablet	Hum
35	Simponi	Solution for injection in pre-filled pen	Hum
36	Simponi	Solution for injection in pre-filled syringe	Hum
37	Stelara	Solution for injection in a pre-filled syringe	Hum
38	Taxotere	Concentrate for solution for infusion	Hum

	Product	Pharmaceutical form	Human / Veterinary
39	Velcade	Powder for solution for injection	Hum
40	Vidaza	Powder for suspension for injection	Hum
41	Vistide	Concentrate for solution for infusion	Hum

Annex 3: List of inspectorates participating in the 2012 programme[3]

Country	National Authority name
Austria	AGES PharmMed
Belgium	Agence Federale des Medicaments et Produits de Santé, AFMPS
Czech Republic	State Institute for Drug Control
	Institute State Control of Veterinary Biologicals
Cyprus	Ministry of Health
	Veterinary Services
Denmark	Danish Health and Medicines Authority
Estonia	State Agency Medicines
Finland	Finnish Medicines Agency, FIMEA
France	Agence Nationale du Médicament Vétérinaire, ANSES
	Agence nationale de Sécurité du Médicament et des Produits de Santé, ANSM
Germany	Zentralstelle der Länder für Gesundheitsschutz bei Arzneimitteln und Medizinprodukten, ZLG
Greece	National Organization for Medicines
Hungary	National Institute of Pharmacy
Iceland	Icelandic Medicines Control Agency
Ireland	Irish Medicines Board, IMB
Italy	Ministerio della Salute - AIFA
	Ministerio della Sanita
Latvia	Health Inspectorate
Lithuania	State Medicines Control Agency
Luxembourg	Ministère de la Santé, Division de la Pharmacie et des Médicaments
Malta	Medicines Authority
The Netherlands	Inspectie voor de Gezondheidszorg
	Nederlandse Voedsel- en Warenautoritieit, NVWA
Norway	Norwegian Medicines Agency, NOMA
Poland	Main Pharmaceutical Inspectorate
Portugal	Direcção Geral de Veterinaria
	Instituto Nacional da Farmacia e do Medicamento , INFARMED
Romania	National Agency for Medicines and Medical Devices
Spain	Agencia Espanola de Medicamentos Y Productos Sanitarios, AEMPS
Slovakia	State Institute for Drug Control
	Institute for State Control of Veterinary Biologicals and Medicaments
Slovenia	Institute of Pharmacy and Drug Research
Sweden	Medical Products Agency
United Kingdom	Medicines And Healthcare Products Regulatory Agency, MHRA

[3] Source:EDQM

Annex 4: List of laboratories participating in the 2012 programme[4]

Country	Name
Austria	AGES-C - AGES PharmMed (Chemicals & Pharmaceuticals), Vienna
Belgium	IPH-C - Scientific Institute of Public Health - Medicines Section, Brussels
Bulgaria	BDA - Bulgarian Drug Agency, Sofia
Cyprus	SGL - Laboratory for the Quality Control of Pharmaceuticals, Cosmetics and Food Suppl., Nicosia
Czech Republic	SUKL - State Institute for Drug Control, Laboratory Control Section, Prague USKVBL - Institute for State Control of Veterinary Biologicals and Medicaments, Brno
Denmark	DKMA - Danish Health and Medicines Authority (formerly Danish Medicines Agency), Copenhagen
Estonia	SAM - State Agency of Medicines, Quality Control Laboratory, Tartu
Finland	FIMEA - Finnish Medicines Agency/ Laboratory, Helsinki
France	ANSM - Direction des Laboratoires et des Contrôles - Site de Montpellier (formerly AFSSAPS-M), Vendargues ANSM - Direction des Laboratoires et des Contrôles (formerly AFSSAPS-P), Site de Saint-Denis ANSES - Agence Nationale du Médicament Vétérinaire, Fougères
Germany	AMI - Arzneimitteluntersuchungsinstitut –Nord GmbH, Bremen BY - Landesamt für Gesundheit und Lebensmittelsicherheit, Oberschleißheim LLBB - Landeslabor Berlin-Brandenburg, Berlin NW - Arzneimitteluntersuchungsstelle NRW, Münster PEI - Paul-Ehrlich Institut, Langen
Greece	EOF - Laboratory Division of the National Organization for Medicines, Athens
Hungary	NIP - Laboratory of National Institute of Pharmacy, Budapest DVMP - National Food Chain Safety Office - Directorate of Veterinary Medicinal Products, Budapest
Ireland	IMB_PALG - Public Analyst's Laboratory, Galway
Italy	ISS-H - Istituto Superiore di Sanità, Roma
Latvia	SAM - Medicines Examination Laboratory, Riga
Lithuania	VVKT- State Medicines Control Agency / Medicines Control Laboratory, Vilnius
Luxembourg	LNS - Laboratoire National de Santé, Service du Contrôle des Médicaments, Luxembourg
The Netherlands	RIVM-B - Centre for Biological Medicines and Medical Technology, Bilthoven
Norway	NOMA - Norwegian Medicines Agency, Oslo
Poland	NIL - National Medicines Institute, Warsaw
Slovenia	JAZMP, Agency for Medicinal Products and Medical Devices, Ljubljana
Slovakia	SUKL, State Institute for Drug Control, Bratislava
Spain	AEMPS-C - Spanish Agency of Medicines and Medical Devices, Chem. and Pharm. Div., Madrid
Sweden	MPA - Medical Product Agency, Uppsala
United-Kindgom	NIBSC - National Institute for Biological Standards & Control, Potter's Bar MHRA - Laboratory of the Government Chemist, Teddington

[4] Source: EDQM