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## Summary

## Summary

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# Promoting the development of medical treatment of rare diseases

An orphan drug signifies an official designation in the European drug supervision. A medicinal product can be designated as an orphan medicinal product if it is intended for a condition affecting not more than five in ten thousand people in the EU. The condition must be life-threatening or chronically debilitating. If the condition is less severe, it is possible to obtain orphan drug status on the basis that the rare use of the product would not cover its development costs.

Another condition for the granting of the status is that the drug is either the only drug used for the rare condition in question or that the product is expected to provide significant improvement compared with the therapies in use at present.

Applications for orphan medicinal product designations are submitted to the European Medicines Agency (EMEA), where the documentation supplied concerning the product will be evaluated by the Committee for Orphan Medicinal Products (COMP).

Since its establishment in April 2000 the Committee has processed about 350 applications. Orphan drug status has been granted to over 200 products, 15 of which had obtained marketing authorisation by June 2004. Of these, bosentan (for pulmonary arterial hypertension), imatinib (for the treatment of certain chronic forms of myeloid leukaemia and gastro-intestinal stromal tumours, GIST) and pegvisomant (for acromegaly) are for sale in Finland.

A developer of a new drug may apply for orphan drug status for his product at any stage of the development, and consequently, a designation once obtained does not guarantee a marketing authorisation. A designation is often applied for as early as at the stage of preclinical studies.

If marketing authorisation is granted for an orphan drug, the marketing authorisation holder has 10-year exclusive sales rights in the therapeutic indication in question, unless superior treatment alternatives can be offered by competitors.

Generic competitors in the area of therapeutic indications of the orphan drug are prohibited for 10 years even when the active substances of several orphan drugs have passed their patent protection period. The status has in that case been obtained on the grounds of a special property affecting the route of administration, duration of effect, etc., which has been used for a familiar medicinal substance to render it effective in the treatment of a rare condition.

The EMEA is to start publishing data about orphan drug marketing applications relating to their active substances, the indications on the grounds of which the authorisation is applied for, and concerning the applicants for the marketing authorisations. This will allow anyone else involved to become familiar as early as possible with the fact that the medical treatment for the rare condition in question may become a special area for which competition restrictions are going to apply for a fixed term.

Orphan drug status is a valuable designation for the developer of a new drug. It serves to demonstrate the fact that independent experts have evaluated the development project and found it to be good. The status will in particular strengthen the confidence in the project by both the drug developers and those investing their money in the development work. Scientific advice and support to orphan drug developers in marketing authorisation issues will also be available from the authorities.

## Summary

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# Treatment of urinary incontinence

*Involuntary passage of urine is a common health problem in women which is associated with impairment of the quality of life. The incidence of the condition is age-related inasmuch as it occurs in 12–42% of young women and in 17–55% of older women. Urinary incontinence occurs in all human races, all social classes and also in men, even though the incidence in men does not increase until after the age of 60.*

There are three main types of urinary incontinence. In stress incontinence dribbling occurs immediately in association with straining, coughing or lifting. About 60% of cases of urinary incontinence in women are of this type, with peak prevalence between the ages of 50 and 55. In urge incontinence, a strong sense of urgency to void is experienced before the involuntary passage of urine. Mixed urinary incontinence is the involuntary passage of urine caused by a combination of both stress and urgency. Overactive bladder is a more recent definition which is associated with a sense of urgency, more frequent need to void, but it is not necessarily associated with awareness of involuntary loss of urine.

### What is the cause?

For the maintaining of normal urinary continence the co-operation of the brain, the peripheral nerves, the connective tissues, the muscles and the hormones is necessary. Disturbed working of any of these functions may therefore impair the ability to maintain continence. In stress urinary incontinence, weakness of the urethra and/or the surrounding supportive structures is present. In urge incontinence, excessive activity of the bladder wall muscle is causing the symptoms. It is not always possible to find an obvious reason for the poor capacity of the bladder to stretch, and it is consequently common to speak of idiopathic overactivity of the bladder wall.

### Risk factors

Obesity is an independent risk factor for urinary and faecal incontinence. The amount of excess weight is related to the quantity of escaping urine. Chronic cough and obstructive pulmonary diseases may impair the supportive structures of the urethra and result in more severe urinary incontinence. Neurological diseases may result in an overactive bladder by disturbing the normal pontine micturition centre. Such diseases include cerebral infarction, Alzheimer's disease, Parkinson's disease, multiple sclerosis and cerebral palsy. Other concomitantly occurring conditions associated with urinary incontinence include constipation, diabetes, depression and back back complaints.

There is contradictory evidence of the effect of hysterectomy on urinary incontinence. The age at which hysterectomy was carried out is of consequence to the symptoms of urinary incontinence. The failure of other supportive structures of the pelvic floor may be associated with urinary incontinence, or urinary incontinence may occur without other symptoms of loss of tone. Problems of micturition may occur following gynaecological reconstructive surgery. Poor contraction of the pelvic floor muscles is a risk factor for urinary incontinence.

### Pregnancy, childbirth and urinary incontinence

Both pregnancy and childbirth weaken the supportive structures of the pelvic floor and may consequently expose the patient to urinary incontinence later in life. Involuntary passage of urine has been reported by as many as 50% of pregnant women. Fortunately, post-delivery urinary incontinence remains a permanent complaint in only 3–11% of women who have given birth. The pudendal nerve lying at the bottom of the pelvic floor may become temporarily or permanently damaged during delivery. The nerve recovers by itself within two months, so the follow-up examination at a maternity health centre should include an assessment of the pelvic floor function. Risk factors for urinary incontinence include the maternal weight, the child's weight, the duration of the expulsive stage of labour, operatively assisted delivery and rupture of the anal sphincter. The first childbirth appears to be the most significant one. A Norwegian demographic study (involving 15,307 women) found that both women who had undergone caesarean section and women who had had

spontaneous delivery had more frequent stress and mixed urinary incontinence than women of corresponding age who had not given birth. Absence of childbirth in a woman's history does not, however, give full protection against urinary incontinence. Emerging risk factors for urinary continence found in a study of women who had not given birth included high body weight, urinary tract inflammation, depression and hysterectomy.

## Ageing and urinary incontinence

Structural defects of nerve, muscle and supportive structures and impaired functions associated with ageing all present a risk for urinary incontinence. The incidences of stress and mixed urinary incontinence increase with age. Despite age-related reduced muscular function and hormonal changes in women, demographic studies do not show increased incidence of stress urinary incontinence. When examining the causes of urinary incontinence in the elderly one should bear in mind any temporary causes that may exist: delirium, inflammation, atrophy/inflammation of the vaginal mucosa, medicinal substances, psychiatric illnesses, increased secretion of urine (heart failure, hyperglycaemia), restricted mobility and difficulties in emptying the bowel.

## What examinations are necessary?

Important details are provided by the patient's own account of how and when the urinary incontinence started and when it most typically occurs. Appropriate questionnaires for this purpose are available from pharmaceutical manufacturers. It is often difficult for both the patient and the doctor to get a picture of the true nature of the complaint. In that case, the patient should be asked to fill in a bladder diary for a few days. Women should undergo a gynaecological examination and men should have their prostates palpated. A clean urinary sample is part of the basic examination.

When the frequency of involuntary passage of urine is less than five times per week, a mild form of the condition is present. More than ten involuntary passings of urine per week is an indication of a severe condition.

## Treatment in out-patient care

Conservative, i.e. non-surgical, treatment can be started when a basic review of the patient has been carried out and a picture of the type of the urinary incontinence established. The conservative treatment consists of: guided pelvic floor muscle training, training of the bladder, electrical stimulation, medical treatment, changes of lifestyle, aids and appliances, and incontinence protection. If the treatment response is good and there is no uncertainty as to the diagnosis, the treatment is continued in out-patient care. For the sake of treatment response, it is important that both the professional offering the therapy and the patient are committed to the therapy.

## Guided pelvic floor muscle training

The pelvic floor muscles assist in closing the urethra provided the muscles are intact and attached to the surrounding tissues. After childbirth and with age, the function of these muscles may be insufficient, and training under the guidance of a physiotherapist may be appropriate. Training the pelvic floor muscles is appropriate treatment of mild or moderate stress or mixed urinary incontinence.

The training should follow the general principles of muscular exercises. In several studies two in three women with stress incontinence have been reported to have benefited from muscular training, even though full urinary control has not been gained by all women (1). With biofeedback devices a physiotherapist can help the patient to achieve the objective of muscular training. With the aid of a biofeedback device the patient is able to listen to the training instructions at home by using headphones while the device is registering the performance.

Vaginal balls can also be used to promote muscular training. It should be borne in mind, however, that results can only be achieved by active muscular work. In general, the method of using vaginal balls has not been found superior to using pelvic floor muscle training alone.

## Electric stimulation

Therapy consisting of electric stimulation has been used in muscular training for the treatment of stress urinary incontinence to relax the bladder contraction function in urge urinary incontinence. Electric stimulation can be used to supplement pelvic floor muscle training and other treatment; but, in stress urinary incontinence it will, however, not convey any supplementary effect to the pelvic floor muscle training.

## Training of the urinary bladder

It is typical of patients suffering from urge urinary incontinence or overactive bladder to micturate frequently, even as often as 20 times a day. Increasingly frequent visits to the toilet will reduce the storage capacity of the bladder. The aim of bladder training is gradually to decrease the frequency of micturition and thereby increase the capacity of the bladder. The patient aims at gradually tolerating the sensation of the urge to micturate. Keeping a diary during the training is recommended. Normally, the micturition interval is 3–4 hours in daytime, and a person of working age goes to the toilet once a night at the most.

In some patients it may also be necessary to review the amount and timing of liquid consumed and the schedule of administration of some agents, such as diuretics, with an effect on the urinary secretion.

## Medical treatment

Anticholinergics are superior to placebos in the treatment of the overactive bladder (2). They decrease the involuntary contractions of the bladder wall muscles. The anticholinergics in use in Finland at present are oxybutynin, tolterodine and trospium chloride. The most common adverse effects of anticholinergics are dryness of the mouth, constipation and difficulty with close vision. Once daily administration of a slow-release formula

drug would appear to have fewer adverse effects. Despite the theory that anticholinergics would impair the memory performance, they are also used in dementia patients when urinary incontinence is a considerable disadvantage.

New medicinal substances for the treatment of the overactive bladder are under study, because its? adverse effects can cause a number of patients to stop using a drug. Acetylcholine is secreted via the muscarinic receptors. The largest quantity of $M_2$ receptors is to be found in the urinary bladder, but it is the $M_3$ receptors that exert the greatest effect on the detrusor muscle contraction. Both darifenacin and solifenacin have been found to decrease the frequency of involuntary passages of urine. In a randomised study (involving 1,077 patients), solifenacin 5 mg or 10 mg administered once daily significantly decreased the number of involuntary passings of urine and the frequency of needing to void it. As a consequence of adverse reactions, 14% and 21% of patients drop out of the treatment (3).

Dopamine, serotonin and norepinephrine (noradrenalin) are nerve transmitter agents which take part in lower urinary tract regulation. Duloxetine has a balanced double effect: it inhibits the norepinephrine and serotonin re-uptake. In clinical studies done so far it has been found to have a dose-dependent effect on the reduction of frequency of involuntary passing of urine superior to that of a placebo. Under trial conditions duloxetine has been found to increase the urethral contractor muscle activity, and it is consequently expected to be of benefit in stress urinary incontinence. Compared with a placebo, the reduction in the frequency of involuntary passing of urine was statistically significant in a study involving 458 women (54% compared with 40%, $p = 0.05$). The most common undesirable effect with the use of duloxetine 40 mg twice daily is nausea and feeling of faintness. Seventeen per cent of the patients withdrew from the medical treatment due to adverse reactions (4).

In postmenopausal women, oestrogen has not been found to decrease the quantity of urine involuntarily passed. Topical treatment of mucosal membrane atrophy with oestrogen in post-menopausal women is nevertheless recommended, because it objectively reduces the number of cases of urinary tract inflammation and the experience of the patients is that it reduces the symptoms associated with the lower urinary tracts.

## When surgery?

Surgery is appropriate in patients with stress or mixed urinary incontinence and in whom conservative treatment has not produced an adequate response and the restriction imposed by involuntary passage of urine is significant to the daily life of the patient. National criteria for surgery in urinary incontinence are expected to be published later this year. The surgical techniques have during the last decade undergone a radical change towards more patient friendly and safer procedures. Using correctly chosen criteria of surgery, nine out of ten women will become dry following day case surgery. Modern surgery aims at preserving the structure of the pelvic floor intact by supporting the urethra with a synthetic mesh. The most extensively studied new surgical method is the TVT (tensionfree vaginal tape) procedure (5), which will soon be accompanied by the introduction of TOT, transobturator tape technique) and TVT-O transobturator TVT (TVT-O, "inside-to-out" suburethral sling for the treatment of stress urinary incontinence (SUI)) procedures. Initially, the results of these procedures are equal to those with TVT, but the leakage and the problems associated with the urinary bladder penetration are less significant.

Several different types of treatment methods have been available for urinary incontinence without thorough preceding investigations. Examples of these include the urethral cap, the type of vaginal support which elevates the urethra, vaginal tampons and various periurethral bulking injections. Practice has shown, however, that only good clinical therapeutic examinations can guarantee efficacy. Treatment of urinary incontinence is rewarding since both the conservative and the surgical treatments are proven to improve the patient's quality of life and restore normal sexual activity (6).

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## Summary



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**SII News**


# The first year of generic substitution

More than 700,000 patients in Finland will have found that one or more of the refundable drugs they have been receiving have been replaced with a less expensive generic counterpart during the first year of generic substitution. The drugs most frequently replaced included antihistamines, antidepressants and lipid-reducing agents. Two-thirds of the cost savings were nevertheless generated by the reductions in price of the medicinal products appropriate for substitution. The savings generated by generic substitution inhibit in particular the increase in drug costs generated by the increased widespread use of new, more costly drugs.

Generic substitution was introduced in Finland in April 2003. This new practice would require the pharmacies to replace the medicinal product prescribed by a doctor with a less expensive generic counterpart unless the doctor prohibits or the buyer declines the replacement. The National Agency for Medicines decides whether a generic counterpart can be substituted for another drug, and the Agency also maintains a list of approved substitutable drugs.

Generic substitution is guided by the so-called price corridor. Prescribed products are replaced with the cheapest or close to the cheapest interchangeable generic or parallel import products. The lowest limit of a price corridor is the lowest price of the substitutable products. The upper limit is achieved by adding EUR 2 to the lowest price, if the least expensive product costs less than EUR 40; or EUR 3, if the least expensive product costs EUR 40 or more. The a price corridor for different groups of substitutable drugs is established quarterly following the price notifications submitted by the pharmaceutical companies.

## Substitutable drug purchases

During the first year of generic substitution, from the beginning of April 2003 until the end of March 2004, there were a total of 12.4 million prescriptions for substitutable drugs that were dispensed by pharmacies and refunded from the health insurance scheme. This is about 45% of all refunded prescriptions during that time. A prescription in this case is the same as one purchase of a drug prescribed by a doctor.

The proportionate cost of substitutable drugs among the total costs of all refunded drugs during the year was about 34%. In April 2003 the proportion was 36% and in March 2004 it was less than 33%. The proportion is diminished by the increasing use of the more recent, more expensive drugs and by price reductions of the substitutable products. The proportion may also increase, of course, when more medicinal substances become substitutable as the patent cover for the original products eventually runs out.

Drugs used for cardiovascular diseases accounted for about 40% of all prescriptions and costs of substitutable drugs (Table 1). Measured by the number of prescriptions, the biggest groups thereafter were anti-infectives and drugs for the treatment of the nervous system.

During the year, about one in eight prescriptions containing a substitutable drug was at the pharmacy replaced by a cheaper alternative. The most common substitutions made were of antihistamines (30% of the prescriptions), antidepressants (27%) and lipid-lowering agents (23%). Substitutions were prohibited by the prescribers in only 0.4% of the cases where substitutions would have been possible, and clients declined to accept a substitution in less than 11% of the cases. The prescribed product in nearly three out of four prescriptions was already within the price corridor, in which case there was no need to replace it.

## Cost savings generated

Generic substitution aims at promoting cost-effective medical treatment. Savings are made both by actually concretely replacing products with less expensive alternatives, and by tougher price competition between pharmaceutical companies. The total savings generated during the first year of generic substitution in Finland amounted to EUR 88.3 million, which is about 6% of the total costs of drugs refunded from the health insurance system during the same period. The clients' proportion of the sum was EUR 39.2 million, and the savings in reimbursement costs payable by the Social Insurance Institution totalled EUR 49.1. The proportion for the health insurance is higher than that for the clients' mainly because a great number of drugs entitled to special reimbursement fall into the category of generic substitution. Over half of the total savings were generated by drugs used for cardiovascular diseases (Table 1). The proportion of the total savings due to substitution was about a third, EUR 28.8 million.

Over half of the savings created by generic substitution came from substituting lipid-lowering agents and antidepressants (Table 2). The cost saving for each substitution was on average EUR 18.39. One substitution involving the product of citalopram saved almost EUR 56, and that of the product simvastatin about EUR 47. Other drug groups where the substitutions created significant savings were, for example, beta blockers and ACE inhibitors.

**Table 1. Prescriptions, costs and savings for substitutable products reimbursed by the national health insurance scheme in 1.4.2003–31.3.2004**

| | Prescriptions | | Costs | | Cost savings | |
|---|---|---|---|---|---|---|
| | In thousands | Share | EUR 1 000 | Share | EUR 1 000 | Share |
| A Alimentary tract and metabolism | 648 | 5.2 % | 28,660 | 5.9 % | 3,650 | 4.1 % |
| B Blood and blood forming organs | 45 | 0.4 % | 1,553 | 0.3 % | 16 | 0.0 % |
| C Cardiovascular system | 4,604 | 37.1 % | 197,790 | 41.0 % | 46,941 | 53.2 % |
| D Dermatologicals | 120 | 1.0 % | 11,882 | 2.5 % | 1,225 | 1.4 % |
| G Genito urinary system and sex hormones | 512 | 4.1 % | 28,984 | 6.0 % | 2,376 | 2.7 % |
| H Systemic hormonal preparations | 47 | 0.4 % | 1,215 | 0.3 % | 5 | 0.0 % |
| J Antiinfectives for systemic use | 2,013 | 16.2 % | 39,715 | 8.2 % | 7,377 | 8.4 % |
| L Antineoplastics and immunomodulating agents | 144 | 1.2 % | 23,880 | 5.0 % | 304 | 0.3 % |
| M Musculo-skeletal system | 1,508 | 12.2 % | 34,760 | 7.2 % | 4,443 | 5.0 % |
| N Nervous system | 1,958 | 15.8 % | 86,994 | 18.1 % | 17,434 | 19.7 % |
| P Antiparasitic products. insecticides and repellants | 20 | 0.2 % | 268 | 0.1 % | 23 | 0.0 % |
| R Respiratory system | 680 | 5.5 % | 23,914 | 5.0 % | 3,846 | 4.4 % |
| S Sensory organs | 92 | 0.7 % | 2,214 | 0.5 % | 660 | 0.7 % |
| All substitutable products | 12,394 | 100.0 % | 481,829 | 100.0 % | 88,300 | 100.0 % |

Source: Prescription Register at Kela

**Table 2. Drug groups and medicines (eligible for reimbursement payments) which generated the most savings through generic substitutions in 1.4.2003–31.3.2004**

| | Cost savings | | Cost savings/exchange |
|---|---|---|---|
| | EUR 1 000 | Share | Eur |
| C10 Serum lipid reducing agents | 7,970 | 27.7 % | 44.59 |
| Simvastatin | 7,613 | 26.5 % | 47.16 |
| Lovastatin | 370 | 1.3 % | 27.51 |
| N06 Psychoanaleptics | 7,905 | 27.5 % | 43.98 |
| Citalopram | 7,312 | 25.4 % | 55.78 |
| Paroxetin | 400 | 1.4 % | 15.91 |
| C07 Beta blocking agents | 4,055 | 14.1 % | 15.77 |
| Bisoprolol | 2,877 | 10.0 % | 15.98 |
| Atenolol | 900 | 3.1 % | 23.81 |
| C09 Agents acting on the renin-angiotensin system | 3,488 | 12.1 % | 26.08 |
| Enalapril | 2,393 | 8.3 % | 29.39 |
| Enalapril and diuretics | 624 | 2.2 % | 23.15 |
| Lisinopril | 451 | 1.6 % | 23.94 |
| R06 Antihistamines for systemic use | 1,242 | 4.3 % | 12.31 |
| Cetirizin | 790 | 2.7 % | 11.13 |
| Loratadin | 452 | 1.6 % | 15.10 |
| J01 Antibacterials for systemic use | 1,107 | 3.8 % | 8.88 |
| Ciprofloxacin | 878 | 3.1 % | 22.45 |
| J02 Antimycotics for systemic use | 756 | 2.6 % | 8.89 |
| Fluconazole | 756 | 2.6 % | 8.89 |
| G04 Urologicals | 583 | 2.0 % | 14.42 |
| Finasteride | 495 | 1.7 % | 16.81 |
| All substitutable products | 28.759 | 100.0 % | 18.39 |

Source: prescription Register at Kela

The greatest cost savings, two thirds of total costs, were created by price reductions owing to tougher price competition. These calculations do not, however, take into account any price changes or generic substitutions in those substitutable drugs which were not eligible for a refund from the health insurance system. Consequently, the actual savings may well be even higher than calculated.

Generic substitution reduced the rate of the growth in the amount of refunds during 2003. The cost of refunds from the health insurance system, totalling EUR 917.5 million, increased by less than 7% compared with the previous year, whereas the increase in 2002 was about 12%. Price reductions of substitutable drugs and raising the top limit of the fixed co-payment from EUR 8.40 to EUR 10 in the basic refund category placed several less expensive drugs outside the refunding system altogether, e.g. some anti-inflammatory analgesics and antibiotics. The number of patients receiving refunds did in fact drop by about 2% in 2003 compared with the previous year.

The first year of generic substitution exceeded all expectations. Clients have in the main been satisfied with the new procedure, and considerable savings have been generated by the system. The prices of individual substitutable products were reduced by a maximum of over 80% in comparison with the prices before generic substitution was introduced. In future, the extent of generated savings and the growth rate of medicine costs will be dependent, for example, on the number of medicinal substances falling in the category of suitability for generic substitution, and the value of their sales.

## Summary



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# Drug classification

According to the Finnish Medicines Act, the National Agency for Medicines decides as necessary whether a substance or a product should be classified as a drug. The decision may be requested, for example, by the product manufacturer, the importer, or the customs authorities.

### Classification criteria

Products are classified in accordance with their composition and the therapeutic indications proposed. The medicinal properties of the composition are referred to in the Agency's list of drugs where the substances contained in Appendix 1 are medicines, the herbal medicinal products listed in Appendix 2 may be classified as medicines, and Appendix 3 lists the vitamin and mineral concentrations which, when exceeded, may classify the product as a medicine.

The purpose of a product is medicinal if it is used according to the specification of a drug in accordance with Section 3 of the Medicines Act, that is, for example, to cure, alleviate or prevent a disease or its symptom. A product or a substance used either internally or externally to identify a condition or the cause of a disease, or to restore, correct or modify the vital functions, in either humans or animals.

Products are not automatically classified as drugs despite the fact that they contain the substances or herbal medicinal products included in the Agency's list of drugs, or that their vitamin and mineral concentrations exceed the limits given in the list. Products are classified as drugs if they have a distinct medicinal purpose although their composition may not be medicinal (e.g. insulin dilution solution). Even though the purpose of the product may not be medicinal, the product is a drug if it can produce physiological changes or pharmacological reactions in the body.

Statements relative to the vital functions or the reduced risk of disease can be made on foodstuffs. Further information is provided in the guide on health statements (Terveysväitteiden valvontaopas, Finnish) published by the National Food Agency (www.elintarvikevirasto.fi)

### Classification and the EU

The national decisions on classification in Finland are also influenced by the Community legislation and the established legal praxis of the European Court of Justice. EU institutions have in their own statements consistently endorsed the principle of free competition and common internal markets aimed at reducing the restrictions which inhibit competition. One such inhibition is, for example, the maximum concentrations of vitamins and minerals which, when exceeded, would automatically classify the product as a drug. According to a decision by the European Court of Justice in April, classifications cannot be designed following pre-set concentration limits; each classification should instead be established individually. National variations are allowed; if a product is not considered a drug in one member state, it may nevertheless be classified as a drug in another member state on the grounds of its pharmacological effects, for example.

However, for most vitamins and minerals, scientific evaluations have not been completed within the EU with the aim of confirming the "maximum values", excess levels of which would pose a health risk. Maximum concentrations, which would make a distinction between a nutritional supplement and a drug, have not been established either. The most recent position paper on the issue of concentrations was nevertheless published last spring. According to the statement of judgement of the European Court of Justice (29.4.2004, case C-387/99), vitamin preparations manufactured and sold as nutritional supplements cannot systematically be classified as drugs when they contain three times the recommended daily dose of vitamins other than those of A and D; the daily dose being that recommended by the German Nutrition Society (Deutsche Gesellschaft für Ernährung).

### After the classification

Once classified as a drug, the product may not be placed on the market as a foodstuff, but instead, a drug marketing authorisation must be applied for. The commercial trader is always responsible for the sale and choice of appropriate channels of marketing of its products. It is also the trader's responsibility to ensure that a product classified as a drug is withdrawn from the shelves of shops selling foodstuffs. The supervisory authorities may interfere with the illegal sale of the product.

**Information on classification is available on the website of the National Agency for Medicines at: http://www.nam.fi/english/classification/**

**Translation Mervi Moisander**

# The Finnish National Agency for Medicines is moving in week 42

The National Agency for Medicines (NAM) moves to new premises in Ruskeasuo at Mannerheimintie 103b, on 14 and 15 October 2004. NAM's laboratory will remain at its present address of Mannerheimintie 166, FI-00300 Helsinki.

The postal address and the telephone numbers to the exchange, to direct lines and faxes will remain unchanged. The postal address is PO Box 55, FI-00301 Helsinki, Finland.

The registry office and incoming mail reception will be on the 4th floor. The goods reception will be past the main entrance on the ground floor on the Nauvontie side of the building.

We apologise for any possible delays in telecommunications during week 42. In urgent cases it is advisable to telephone directly to a mobile phone number or to transmit faxes to (intl. +358 9) 714 469).

We hope that visits to NAM during and immediately after the move will be kept to a minimum, and that application material and other goods are addressed to our new premises as of the following weeks.

During the move, our mobile phone numbers will be operational.

***Pharmacovigilance Department, (intl. +358 50) 552 1091 (urgent pharmacovigilance matters)***

***Marketing Authorisation Department, (intl +358 50) 511 4031***

***Enforcement and Inspection Department, (intl +358 50) 561 2680 (product defects, medicines' manufacturing and distribution)***

***Laboratory, (intl +358 50) 302 2709***

***Medical Devices Department, (intl +358 50) 563 8532 (adverse incidents)***

***Administration Department, (intl +358 50) 520 3126 (invoices, access control, security)***

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*Liisa Kaartinen, (intl +358 50) 565 8104 (Veterinary medicine)*

*Seija Ahonen, (intl +358 400) 467 719 (IT matters, telephonic communications)*

*Katja Lindgren-Äimänen, (intl +358 50) 511 1657 (Press)*

Centre for Pharmacotherapy Development will have offices on the 4th floor of NAM's new premises. The centre's telephone and fax numbers will remain unchanged. The visiting address will be Mannerheimintie 103b, FI-00300 Helsinki, Finland. The postal address is PO Box 55, FI-00301 Helsinki, Finland. Manager Taina Mäntyranta's mobile phone number is (intl +358 50) 5812769

**Translation Sari Jay**