prevailed symptoms, treated by them are: headache, cold, flue, pain, migraine, toothache, etc. The great part of the consumers read carefully the leaflets before the drug application, but they consider the obtained information as insufficient.

Conclusion: Consumers' sources of information are mainly pharmacists, medical doctors and TV advertisements. The pharmacists obtained the necessary information from manufacturers' advertisements and from the medical representatives. Our suggestions for improvement of the OTC-analgesics knowledge are:

— follow-up education programs for pharmacists about the common symptoms and diseases;
— developing a Pharmacovigilance system;
— study the readability of the PILs and determine the minimum necessary information that must be included.

P016. Pharmasearch: a network of pharmacovigilance between Italian GPs

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Aim of the Study: To promote the spontaneous ADR reporting system in Italy (institutional aim).

To improve the quality of prescriptions, through a both individual (single reporter) and collective (network of reporters) mechanism of evaluating the risk/benefit ratio of pharmacological treatments (educational aim).

Methods: Since January 1st 2002, a collaboration started between the Department of Medicine and Pharmacology of the University of Messina (Co-ordinating Centre) and a group of GPs of the Italian College of General Practitioners (SIMG) (n. 126 till April 10th 2002) which voluntarily accepted to take part to the Pharmasearch network.

Every GP participating has been asked to send to the Co-ordinating Centre a copy of every ADR reporting form immediately after it has been sent to the competent pharmacovigilance office (as requested by law), any time he suspects an association between a drug and an adverse event occurred in a patient.

The Co-ordinating Centre, after receiving the form, provides the physician with a personal and qualified comment to the ADR reported, according to data retrieved from international literature and on-line database. A causality assessment of each ADR (based upon Naranjo algorithmic rating scale) is also provided, together with a comment on the completeness of the data filled in the reports. Data collected are recorded by the Pharmasearch office in an ADR database for subsequent analysis.

A bulletin about the state of art of the network is generated for the physicians participating every month and quarterly, with a brief description of ADRs reported and drugs involved.

Results: During the first three months of the year, 99 ADRs were reported. One hundred twenty-two medications were implicated as "suspect" drugs for the ADRs. The reporting rate was 74% for Northern regions, 20% for Centre and 6% for Southern regions and islands.

Central Nervous System (24%), digestive tract (20%) and the skin (18%), were the body system most commonly involved. Patients over 65 years of age comprised 48.5% of this series. After causality assessment, 55.5% of the cases were rated as probable and 44.5% were rated as possible.

Conclusions: Although the number of spontaneous adverse reaction reported is small, the network shows promising for future involvement of a growing number of GPs in the pharmacovigilance system.

These preliminary results also confirm the importance of a feedback to reporters in order to stimulate ADRs reporting. Training courses will also be programmed annually, according to the topics of major interest coming out from reports gathered.

P017. Selective reporting on Isotretinoin might be invoked by media attention

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Introduction: Isotretinoin (Roaccutane or Accutane) is a retinoïd, the 13-cis isomer of all-trans-retinoic acid (tretinoin) and a derivative of vitamin A. It is indicated for the treatment of severe, scarring forms of acne. The drug was first approved in 1982. Adverse drug reactions (ADRs) resemble the hypervitaminosis A syndrome that includes mainly, beside teratogeneity of all retinoids, mucocutaneous side effects, liver toxicity and abnormalities of serum lipid profiles. In the early 90s incidental case reports of depression upon isotretinoin use emerged in dermatological journals. There seems to be an enormous increase in both the number of reports on isotretinoin as well as the proportion of reported depression and suicide attempts on isotretinoin following some major publications after 1995. The question raises if there is a correlation between the reporting behaviour and publications in international journals.

Aim of study: Spontaneous reporting systems receive their reports as a subset of possible adverse reactions filtered by the 'reporters attention and judgement'. This investigation addresses the effect of publication and knowledge on reporting behaviour of certain ADRs.

Methods: Reports sent to the WHO Uppsala Monitoring Centre concerning 5 different acne medications (acitretin, benzoyl peroxide, isotretinoin, minocycline and tretinoin) were analysed for the psychiatric disorders: depression, depression aggravated, suicide and suicide temptation/ideation over the years 1988–2001. Time points of publications in the international literature (Medline) and

by the FDA and pharmaceutical industry served as markers for media attention.

Results: Between 1989 and 1995 the WHO-UMC received 1761 ± 356 (mean $\pm$ SD) reported ADRs on isotretinoin per year. The relative occurrences of depression and suicide attempt were stable at 1.86 ± 0.49 and 0.40 ± 0.16 percent. For minocycline only 11cases (0.3%) of depression were reported. After 1995 the number of ADRs progressively increased 2.5-fold in 1999. The relative contribution of depression and suicide attempts on isotretinoin rose to 5.4 and 1.9% respectively. Although some case reports on acute depression were published in 1990 and 1991 in dermatological literature, the first publication in psychiatric literature by Byrne and Hnatko emerged in November 1995. Subsequently the FDA warned and a 'dear doctor letter' was issued in February 1998. The yearly number of reports on acitretin, benzoyl peroxide, minocycline and tretinoin remained stable. Unfortunately worldwide prescription numbers are not available but where increased prescription may increase the number of reported ADRs it is unlikely to explain the changes in proportion.

Conclusion: The number of reported ADRs and the proportion of reported cases of depression and suicide attempts on isotretinoin has been stable until the first major publication 1995. From that time the numbers of ADRs on isotretinoin as well as the proportion of the events depression and suicide attempt have increased several folds. The tight correlation between media attention and the focus on depression and suicide attempts on isotretinoin use and the received numbers of reports including these ADRs is remarkable.

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P018. Preparing for a European pharmacovigilance regulatory inspection

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Guidelines have recently been published stating the role of European agencies in monitoring compliance of companies with pharmacovigilance regulations and indicating that inspections may be performed to ensure that legal obligations are being met. To date, there is little experience in Europe of pharmacovigilance inspections post-marketing, although these have been performed as part of GCP audits in the clinical research setting. In the USA, there has been extensive experience of regulatory compliance inspections: however, the approach in Europe is likely to differ.

This paper looks at preparation for compliance inspection from a European perspective.

Preparation for a regulatory inspection should begin with implementation of routine good practices: preparation of detailed SOPs covering all aspects of pharmacovigilance, training of all staff on SOPs, documentation of training, maintenance of SOP files.

SOPs and / or working practice manuals should include definitions of terms and details of what duties and responsibilities are to be carried out, when, how and by whom. They should include a corporate policy statement on pharmacovigilance; procedures for SOP management; procedures for receipt and handling of AE reports including via medical information enquiries and medical representatives; follow up of ADR reports; expedited ADR submissions; preparation of PSURs and submission; literature screening; signal detection and management; implementation of core safety information; management of new safety concerns; crisis management; interactions with regulatory authorities; database management; third party agreements; training needs; filing and archiving. Where appropriate, there may need to be SOPs documenting the approach to safety surveillance in clinical trials: statements for inclusion in study protocols; details of handling of serious AE reports from trials; processes for identifying new safety concerns and reporting these to investigators and ethics committees.

Documentation and records are of prime importance. Depending on whether this is a headquarters or affiliate office: adequate recording of contacts with reporters of AEs, correspondence files, recording of faxed submissions, maintenance of a tracking register of AEs received and reported, reasons for any late submission of expedited reports, copies of all PSURs submitted, a register of all PSURs, with the data lock points and the dates of submission to regulatory authorities, a register of all enquiries from regulatory authorities, a file with current SPCs for all products with a marketing authorisation in each country should all be maintained.

Meticulous planning regarding pre-arranged site inspection visits should ensure that all staff are suitably prepared and that appropriate facilities are available to assist the inspector. Preparation of a document summarising the work and structure of the relevant parts of the company is important. Notification of various parties in the company of the occurrence of the inspection is necessary.

After the inspection, a report should be prepared based on the inspection findings together with recommendations and an action plan, documenting also any points of disagreement with the outcome of the inspection.