While the Italian Ministry of Health and the US Secretary for HHS were signing an important agreement regarding research in the biomedical field in Washington, AIFA and Dr. Margaret Hamburg, Commissioner of the U.S. Food and Drug Administration were meeting in Rome after signing an important agreement last December. Moreover, the two Agencies agreed on a very important principle: always bring science into the regulatory world, in order to provide best chances for drugs’ efficacy and safety for the patients. This is relevant to the topic I was assigned today.

Life expectancy in Europe has been increasing in recent years, especially in women, showing a striking difference between females and males. However, this difference decreases when we consider the healthy life expectancy.1

Comparing the disability-free life at age 65, among European countries, Italy ranks first, with females still living longer than males, but with a difference reduced to approximately 2 years. As you see in Table 1 the disability-free life expectancy at 65 for males is about 12 years, while for females is about 14 years. These years of life expectancy with disability mean poor quality of life and all the social related problems. 2

This issue has to do with pharma. Looking at utilization and expenditure of reimbursed medicines by age classes in Italy in 2009, the total expenditure and the defined daily dose (DDD) per 1000 inhabitants, for patients between 65 and 75 years, represent more than one fourth of the whole expenditure. Moreover the total expenditure, for patients at 75 years and over, is 31%, making a total of about 57% in the elderly age (> 65). (Table 2) The same figures apply to total DDD of reimbursed medicines: for patients over 65 years is 62%. 3

It is undoubtedly interesting to take a look at the issue of polypharmacy. The percentage of patients under age 45 with more than five prescriptions a year is only 7%, while 45% of the people over age 65 have more than five prescriptions a year. (Table 3) 4

The relationship between polypharmacy and underprescribing is another very important issue. First of all, polypharmacy, that is utilization of many medicines, is common among the elderly. Underprescribing is also frequent in later age. It has been demonstrated that there is underprescription whenever people - usually elderly patients - use many drugs. This may reflect the psychology of the doctor and especially of the general practitioner. Therefore optimizing polypharmacy includes avoiding underprescription.

In a paper published in the British Journal of Clinical Pharmacology in 2007 it was shown that 43% of patients who used five or more medicines are undertreated and in undertreated patients there is a mean of 1.4 medicines lacking. The probability of underprescription increases with the number of drugs used.

The elderly patients are prone to develop iatrogenesis and often they are affected by comorbidity, disability and polypharmacy. Sometimes also the best specialist forgets the holistic concept of medicine, extremely important in this type of patients. These individuals are excluded from clinical trials and therefore the findings cannot be extended to this
category of patients. Eminent geriatricians have called for the conduction of appropriately designed trials involving real geriatric patients.

In a paper by Spinewine et al. 6 appeared in The Lancet, a question was raised: “Appropriate prescribing in elderly people: how well can it be measured and optimized?” The article claims that information technology has the potential to improve and rationalize drugs prescription.

According to the authors, prescribing “in the future could use three crosslinked databases - the patient’s drug history, a scientific drug information reference and guideline database, and clinical information that is patient-specific.” 6

The conduction of properly designed trials involving real geriatric patients is probably the only feasible strategy to accrue the relevant information that can help in difficult decision about optimizing drug treatment in frail older patients, while minimizing the risk of iatrogenesis. This new approach to pharmaco-epidemiological research does require innovative methodology, interdisciplinary integration of multiple experts. AIFA has set up a working group, called “Geriatric Working Group”, for redesigning the pharmacological research in older individuals. 7

Doctor Margaret Hamburg and Doctor Francis Collins, the leaders of the Food and Drug Administration (FDA) and the National Institutes of Health (NIH) wrote a remarkable paper in the New England Journal in July 2010: “A Shared Vision of Personalized Medicine” 8. It claims that the success of personalized medicine depends on having accurate diagnostic tests that do identify patients who can benefit from the target therapies. The old system of the blockbuster is disappearing. The scientific regulatory structure does need to support this growth and understands that science has to come into the regulatory world. FDA is developing the regulatory science standards and evidence needed to use genetic information, in drugs, in device development and in clinical decision-making. The goal is giving to the agencies and companies “a better understanding in applying pharmacogenomic information to drug development” 8.

What’s the perspective? It is the collaboration between regulators, third party payers and scientists, in order to define and design clinical trials based on knowledge, on technology, integrated development of new biomarkers, new medicines, new rules and guidelines. The percentage of patient population for which a drug class is ineffective, is 38% in the antidepressant category and even 75% in the cancer drug. Therefore “One size does not fit all” 9.

The future is really “future which is running so fast”. Only a few years ago, in order to know the sequence of 3.5 billion bases, we would need 13.5 years to sequence. Today, only six years after, we need only one week. The target therapies introduce a lot of advantages: discriminating potential responders from no-responders, identifying which patients are likely to benefit earlier in the disease pathway, ensuring appropriate dosing, reducing incidence of adverse events and in particular improving overall health gain. Hopefully in the future, healthy life expectancy is going to increase and overtake life expectancy with disability.
References

3. AIFA. OsMed-HTA Unit.

* The Italian Medicines Agency, AIFA, is the National competent Authority responsible for all the activities related to the drug regulatory process in Italy: from drugs registration and commercialization, to the check of production sites and manufacturing quality; from the verification of drug safety and appropriateness of use, to pricing and reimbursement. The Agency also supports the Italian Government as high scientific and technical advisor on drug policy.

More specifically, the Agency:

- guarantees access to medicines and their safe and appropriate use as means to protect public health;
- ensures unity of the national pharmaceutical system in agreement with the regional authorities;
- ensures innovation, efficiency and simplification of the marketing authorisation procedures, in order to grant rapid access to innovative drugs and to drugs used for rare diseases;
- provides drug expenditure governance in the framework of economic and financial viability and competitiveness of the pharmaceutical industry
- cooperates with the Regional Authorities in order to maintain the pharmaceutical expenditure in balance with the cost cap annually established by the Government
- encourages investments in research & development in Italy.

AIFA’s aim is to set fair pharmaceutical policies and to assure their consistent application nationwide, at the same time promoting public health and a new pharmaceutical culture and knowledge.