Personalized medicine and treatment of rare disorders as a strategic approach of the development of healthcare till the year of 2020

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Part I. Diagnosis and treatment of rare diseases – unsolved problem of modern medicine

It is formed historically that national medicine is generally focused on common and well-known socially relevant diseases. Patients with rare disorders are one of the most severe problems of the healthcare system (not only in Russia). Diagnosis of such diseases is often difficult or unavailable, treatment is non-effective because of the lack of appropriate drugs (methods of treatment), and prognoses are poor.

A «paradox of rarity» consists in such fact that «diseases are rare, but patients with rare diseases are numerous». It is likely that rare diseases reach 6-8% in the world population of people. Therefore «it is normally to suffer from rare disease». Rare diseases may occur in every family, anytime. It is not only «something terrible, that happens with others». It is cruel reality that may become with every person or with his child. Rare diseases affected such famous people as composer Ludwig van Beethoven, painter Henri de Toulouse-Lautrec, president of USA John Kennedy, tsarevitch Aleksey – son of Imperator Nikolaj II.

According to expert estimates there are about 5-7 thousands life-threatening rare diseases in the world. This number includes exotic disorders such as Kabuki syndrome (300 cases in Europe), Pallister-Killian syndrome (30 cases in Europe), progressive osseous heteroplasia, Niemann-Pick disease, Gaucher disease and more frequent such as mucoviscidosis, hemophilia, different forms of cancer, myeloma, Alzheimer's disease, amyotrophic sclerosis, Huntington's disease etc. But this is not only «exotic». Rare diseases also enclose systemic lupus erythematosis, antiphospholipid syndrome, juvenile rheumatoid arthritis, myasthenia, Guillain-Barre syndrome, primary biliary cirrhosis, lipoprotein glomerulopathy and other known disease.

Each brunch of medicine includes rare diseases. Approximately 80% of these rare disorders have a genetic origin. Other cases are neoplasms, infections (bacterial or viral), allergic reactions, result of exposure of harmful factors of an environment.
The number of rare disease constantly increases (5 new pathologic conditions appear every week in the world). It deals with improvement of the diagnosis and deterioration of ecological situation on the planet which is due to human activity. (New menace is presented by hasteful experiments with genes – synthesis of products with modified genes, cloning etc. People don’t estimate all consequences of such experiments including late effects and can’t neutralize it, what is dangerous).

The government of different countries finances special programs to make the release of «unprofitable» or «orphan» drugs efficacious and business of pharmacologic companies was not detrimental. In many countries special legislative acts were passed to vest benefits for operating companies and to stimulate interest of science and business to innovative projects in this area. These stimuli may be presented by: exclusive marketing license for a term from five to ten years; complete or partial paying of procedures of getting of the official allowance for drug usage; possibility to obtain a financial support for investigations of rare diseases from public funds; informational and organizing support in the drafting of protocols of clinical investigations etc.

USA was the first country being tried to solve this problem. In 1982 special department was formed in Food and Drug Administration (FDA USA) meant for development of «rare products» (Office of Orphan Product Development). Special low – Orphan Drug Act was enacted in 1983 to regulate status of rare disease, orphan drug and to confirm appanage for operating and manufacturing companies, at that was related to not only pharmaceutical and biological drugs, but also medical equipment and dietetic products. According to this law about 1600 known diseases and syndromes were admitted as rare and 300 drugs were concerned to orphans. In the following such legislative acts were passed in other countries – in Singapore (1991), Japan (1993), Australia (1997), South Korea, Canada, Taiwan and in the end in European Union (1999). Currently in many countries drugs that are related to category of rare medicines compose the whole segment of drug market with its rules of production, registration, government support, patent protection etc.

Fundamental documents in European Union were presented by decision of European parliament № 1295/1999/EU from April, 29 1999 and guideline of European parliament №141/2000 from December, 16 1999. These documents enclosed definition of orphan-diseases and orphan drugs and prospects of its research and treatment. In April 2000 according to European guideline Committee for Orphan Medical Products was formed in London (COMP) and it included respective group of patients. This committee must examine drug folder on term till 90 days, and European commission must take a decision during 30-day period about its usage in the territory of EU. According to establishment of EU commission №847/2000 from April, 27 2000 drug register was created for treatment of rare diseases. Till February 2007 status «orphan drug» was assigned for 450 drugs and this decision was made for 34 countries of EU. As explained by president of EURORDIS Terkel Andersen currently number of patients with rare disease reaches 30 million of people in countries of EU, i.e. every 15th European suffer from rare disease. Some of these patients had been waiting for 25-30 years before correct diagnosis of their disease was made.
Materials of European database of rare diseases from 35 countries show the level of efforts being executed in European Union. As on March, 15 there were registered **7242 rare diseases** and pathologic conditions, **1233 clinical laboratories** where a **diagnosis of 1504 rare diseases** is performed, **2003 research laboratories** which perform **4198 projects** in 2040 rare diseases, **283 registers, 3092 expert clinics, 1739 patient organizations, 10302 medical specialists, 521 drugs** are used in treatment of rare diseases.

**Part III. Problem state in Russia**

Situation with organization of the medical and social care of patients with rare diseases in Russia is still very difficult. Medical care in our country is focused on management of socially relevant disease, but individual person with rare disease is face to face with his disease. Current system of the medical care works for more or less socially relevant group of patients and doesn’t embrace rare disorders. Furthermore, problem is not obvious because of absence of diagnosis and registration of such patients. Meantime in according to data of All-Russian population census in 2002, data associated with medium occurrence of rare diseases in population at least 1% of Russian people – about 1.5 million – suffer from these pathologies. In more careful diagnosis this number may reach 8-10%. (For comparison: in according to data presented by Center of demography and ecology of the Institute of economical forecasting of the Russian Academy of Sciences currently in Russia about 2.1 million of people suffer from diabetes mellitus). Why isn’t this problem social?

The first step in organization of medical care of patients with rare disease is correct diagnosis. Specialists in healthcare often don’t have enough experience in the majority of rare diseases (this problem occurs not only in Russia). Absence of information underlies misdiagnosis and this is the source of suffering of patient and his family, cause of the delay of appropriate medical care leading to irreversible consequences.

Diagnosis of rare diseases applies in some laboratories of the research institutes and universities in Moscow (about 200 diseases) and St. Petersburg (several tens of diseases) and is not available in regions. Mass screening of newborns realized within the National project «Health» comprised only 5 diseases (fenilketonuria, congenital hypothyroidism, galactosemia, adrenogenital syndrome, mucoviscidosis) what is precious few in comparison with total number of hereditary diseases.

Patient needs an administration of the appropriate treatment after correct diagnosis of his disease. For this purpose in our country special drug must be registered and specialized medical center must be organized where this treatment may be available (in-patient or out-patient department).

Patient with rare disease may buy required drug or take it for free if he is related to benefit category of patients having a right to social benefits (**patients having a right to additional pharmacological support**) in according to Federal law №122-FZ from 22.08.2004 – «federal benefit persons»; **patients having a right to concessional pharmacological support in according to regional legislative acts** – «regional benefit
persons») and/or suffer from diseases included in state program of pharmacological support of patients with 7 expensive diseases that had been realized from 2008.

Unfortunately in practice it is not so rational especially in case of rare and expensive drugs. Standard of the expenditure of budgetary funds for one patient in month in according to program of additional pharmacological support from April, 1 is 423 of rubles herein that in some cases sums is about 1.5 million of rubles are needed. Finally it leads to extreme deficit of the financial support of program, stable items out of stock of expired recipes in pharmacies, insufficiency of vital drugs and social discontent leading to increase the number of patients who refuses from facilities (in some regions the number of some patients is more than 60%).

Patient must have status of invalid (disabled person) to get a drug within federal program of additional pharmacological support. What does it mean? At first it means that patient can’t be administered a treatment at earlier stages of the disease when it is most effective, and only once he becomes invalid, he can. At second, when situation is reversible and treatment leads to considerable improvement of patient’s condition, patient can’t deny from status of invalid, because then he looses his rights on getting of free drugs. In the result of this prevention of disability changes on its cultivation (it should be stressed that it is related to only several diseases).

Program «7 nosologies» was organized to correct this situation and separate financial support of expensive drugs as individual project. Its own budget reaches 33 billion of rubles in 2008 (sum is compared with budget of additional pharmacological support in 2007). Result was apparent: assurance in expensive drugs became more planned and regular, delays with getting of drugs in the pharmacies are not observed, and want of drugs is satisfied. Problem «expensive-cheap» and associated with it change of care of one patient or treatment of many patients was partially resolved. Debt to manufacturing companies of drugs was decreased and many companies returned on the market.

But this results in new problems. Order of forming and control of the register of patients and compilation of precise system of claims in according to real requirements is not defined, and currently about one third of drugs is unclaimed with the assumption that some patients take a medicines in decreased doses or don’t take it. System of enrollment of new revealed patients in program hasn’t also been formed. Finally some of these patients wait appropriate drug (often unique) for 6 months because tenders for purchase of drugs and collection of claims from regions are performed once in 6 months and chance to be enrolled into the program in other time is minimal. Many of diseases are severe and progressive and after 6 months may contribute more high doses of drugs (new complications of the disease) or patient may not take this drug. Precise system of the monitoring of results of treatment is absent and standards and protocols of management of patients are not developed or are not applied in practice. System of taking drug by patient, its usage and monitoring of results of treatment is needed to be reformed. Patient takes the drug by recipe in the pharmacy, bring it home and put into the cooler, and question about drug assurance and storage conditions of «thermosensitive» drugs arises. The majority of drugs requires administration within the hospital, but hospitalization for several times for months (and often for life) is very difficult and burdensome as for a patient as for a doctor. Furthermore, in many cases
(especially in outlying regions) doctors refuse to make an injection of rare expensive drug because of insufficient experience, absence of knowledge in this area and fear of the development of possible adverse reactions (complications). Finally patients have to come to the central clinic from far (it is financial and physical problem for some of them) or ask for familiar medical workers make an infusions of drug at home for additional payment. Result is wrong frequency and technology of usage of the drug, high risk of complications and decrease of the drug effectiveness.

Of course individual program for rare and expensive nosologies is a great step forward. But we should remember that these diseases are numerous and not only 7 and many of them are curable at the present time. But budget for next 3 years has already been made-up and it doesn’t provide financial support of new orphan drugs. Furthermore current discussed conception of the development of native medicine for the period till year of 2020 doesn’t include theme of rare diseases and orphan drugs. And now words of women who’s daughters-twins suffer from mucopolysaccharidosis type I are actual as never (this disease is treated in all over the world, but not in Russia) – «I am so tired to live side by side with death!..».

In dependence of the disease main method of treatment is presented by special diet (fenilketonuria, galactosemia), administration of drugs in tablet form (congenital hypothyroidism), infusions of expensive drugs (Gaucher disease, hemophilia, primary immunodeficiency), periodic expensive procedures (LDL-apheresis in homozygote family hypercholesterolemia) etc. Patient should take careful monitoring and if it is necessary should be hospitalized in specialized medical center (often federal) where monitoring of used therapy in accordance to approved protocol is available (if protocol exists). Currently patient may take a hospital treatment in such center in the presence of quota (government order) for high technologic medical care. For this possibility disease and medical center must be included in order of Ministry of Public Health and Social Development of Russian Federation about high technologic medical care being published approximately once in a year. Process of getting of quotas (as all procedures deal with financial disposition) is associated with several difficulties and delay, therefore in absence of predictable group of patients medical center is not interested in getting of such quotas. Alternative of this variant for patient is paid medical care (for instance: intravenous infusions of immunoglobulin in adult patients with primary immunodeficiency, as quotas are only for children).

Absence of continuance of the system of healthcare in children and in adults is a serious problem in our country. For example child with rare disease took appropriate treatment till age of 16-18 years; his or her physical and mental development was satisfactory. Then treatment was stopped (because child became adult person with other benefits), in the result of this decompensation of the disease developed and patient was die after some years. So all efforts in his treatment in childhood were vain. Difficult and complicated system of the financial support of healthcare (financial support from different sources), different «schemes» of getting of drugs, different requirements for prescriptions, different pharmacies, necessity to buy privileged drugs of coarse has a negative influence on the effectiveness of treatment of patients with rare (and not only rare) diseases and on the rationality of the usage of the funds committed for this and lead to the increase of social discontent and tonicity.
The simplest method is an administrative division of responsibility: financial support of one type of drugs or methods of treatment (usually more expensive) should be provided from federal budget, other – from regional, and within different programs. In practice it leads to forming of immense attackable system of drug assurance at least for some categories of patients and make complex system of their treatment impossible. Failure of this system at any stage (delay of the incoming of appropriate drugs from central parts, absence of funds for purchase of drugs in regions, impossibility to perform monitoring and correction of used therapy in clinics and so on) results in loss of time, decrease of the effectiveness and «productivity» of treatment and as a consequence development of invalidity, reduction of life expectancy and lowers possible compensation from budgetary funds committed for treatment.

In some cases such situation hinders the development of new modern medical technologies in healthcare. An example is a treatment of myasthenia and Guillain-Barre syndrome. The main method of treatment of severe forms of these diseases in our country is replacement of patient’s plasma on donor plasma to decrease blood level of pathologic antibodies. Worldwide modern selective technologies of blood processing are used instead the replacement of plasma during more than 10 years. Such technologies are also available in our country (cascade plasmapheresis), furthermore their cost is lowered now (approximately twofold) and it is more less than cost of replacement of plasma. But implementation of the method of cascade plasmapheresis is unprofitable for hospitals because decrease of expenses for donor plasma (are financed from other sources) lead to rise of expenses for expendable materials (are financed from hospitals funds). Another advantages (economy in deficient transfusional media, decrease of risk of hemotransfusional infections) don`t take into account.

If drug is not registered patient has a chance to take a treatment only within program of clinical trials with some new drug because legislation of Russian Federation (law «About drugs») creates that unregistered drugs may be imported in country only for clinical trials. Main disadvantages of this variant are unpredictability of treatment results (for example patient don`t know if he takes a drug or placebo within placebo-controlled clinical trials) and limited period of treatment. All trials finish one day, but what will be further?

Current situation is in contradiction with convention of World Health Organization (WHO) stating that every person has a right to adequate treatment and WHO gives a permission to use drugs registered in other countries if patient and his doctor take the appropriate responsibility.

Order of Ministry of Public Health explains that drug may be imported in vital indications in accordance to rules of Ministry. But in practice if drug is not registered it is impossible to start a treatment.

In this case patient (or his relative) may buy drug in other country and bring it home for personal use. This is probable if patient can buy it in other country and doctors in local clinics agree to use it (the last is virtually impossible).

Another variant is getting of drug for free within humanitarian aid from international charitable organizations. But it is also accompanied by different
difficulties and barriers if drug is not registered in Russia. It is impossible for patient
to get a drug without tax payment and customs duty even if drug is vital for him and
he don’t have a choice and time for waiting. We have organized transport of drugs
within humanitarian aid for patients with rare diseases (Fabry disease, mucopolysaccharidosis) for 3 times. Process lasted from 3 to 6 months and required
many different agreements and permissions. Only outgoingness of people taken apart
in this – from Ministry of Public Health to customs office – helped us to perform our
action. The main reason of such difficulties is absence of correct rules of import and
usage of unregistered vital drugs. There is a legislative act «Statute about order of
usage of drugs in patient in vital indications» being admitted after approval of order of
Ministry of Public Health № 494 from 9 of August 2005 and regulating these
procedures, in practice it works only in exceptional cases and causes many questions
because «order of usage» is not clear and complete. But there are also prohibitory laws
(for instance article 22 of a law «About drugs») that are accepted «to fight» against
illegal import of drugs under the pretence of humanitarian aid, and these laws
unfortunately lead to impossibility to provide a medical treatment with vital and
unique drug in many patients with rare disease. It is more simple method to prohibit
something instead to try to solve the problem of individual person.

What does hinder registration of rare (and not only) drugs in our country? An
answer consists in that process of registration is very complicated and difficult
procedure and in practice it lasts for much time and requires great efforts, time and
financial means from manufacturing companies. Therefore the majority of companies
don’t hasten and register their medical products in Russia, particularly companies
producing “orphan-drugs”.

It should be noted that at the present time situation improves. Federal agency for
control in Public Health and social development in accordance with item 10 of article
of a Federal law 19 “About drugs” develops a Statute about accelerated procedure of
state registration of drugs (Information notice of Federal Service for the Supervision of
Public Health and Social Development from 18.12.2008 № 01 I-53/08). It concerns
about drugs using for treatment of rare disease, some epidemic dangerous diseases,
diseases associating with high percent of mortality and invalidity.

Procedure of accelerated registration was applied March, 6 2008 and certificate
about state registration was issued for drug Elaprase using for long-term therapy of
patients with Hunter's syndrome - mucopolysaccharidosis type II. This event is a
“victory” of mother of sick child – Snejana Mitina – and all people helped her. This
event is significant for our country because it was registered a drug for very rare
disorder. Currently in accordance to data of Society of patients with
mucopolysaccharidosis and laboratories of hereditary diseases of metabolism of
Medicogenetic scientific centre of Russian Academy of Medical Sciences there are
about 40 children with this disease in Russia although on the ground of frequency data
in Russian population this number must reach minimum 150. Unfortunately this
positive example of the accelerated registration is still exception then principle. For
instance children with other type of mucopolysaccharidosis (type I) wait for drug
Aldurazyme for several years. Some of them may not already need it…
Theme of rare diseases and rarely used medical technologies was discussed for the first time in 2005 by Formulary Committee of Russian Academy of Medical Sciences with Andrei I. Vorobjev at the head. In 2006 Formulary committee accepted Temporary provision about order of forming of list of rarely used medical technologies and defined the term “rarely used medical technology”. Medical technologies related to category of rarely used technologies must respond high level of evidence of the effectiveness and vital necessity (without its administration in life-threatening diseases and syndromes progression of the disease or deterioration of its coarse, complications or patient’s death may develop) and must rarely used (quantitative criterion of rarity is usage (real or forecasting) of medical technology in less then 10,000 people in Russian Federation). Meantime there was formed and published List of rarely used orphan medical technologies of Formulary committee in second edition of Guidance of medications of Formulary committee (edition 2007 includes only 36 technologies).

In December 2007 there was started organization of Professional service in Formulary Committee for rare expensive diseases. Coordinator of Professional service is Pavel A. Vorobjev. It is suggested that such service will exercise expert-methodic functions and incorporate practicing physicians, research workers, managers of healthcare, representatives of patient’s societies, representatives of pharmacologic companies, laboratory specialists, specialists in nursing care, lawyers etc. Purpose of its formation is public monitoring of realization of program “7 nosologies” (hemophilia, mucoviscidosis, pituitary nanism, Gaucher disease, myeloleukemia and other hemoblastoses, multiple sclerosis, condition after organ and (or) tissue transplantation), estimation of the dynamics of patient’s life quality, their satisfaction in drug assurance and medical care in general, improvement of medical and social care of patients. Program “7 nosologies” was supported by considerable funds (about 1 billion of Euros on 2008), drugs were purchased in two-fold, but mechanism of getting of drug by every patient is needed to be worked in practice. Currently protocols of control of such patients and federal register are produced, claims on drugs are collected and corrected.

Summing up all above said we can make some main conclusions existing at the present time in our country and deal with medical care of patients with rare disease:

1. Absence of relevant register of patients with rare diseases (medical archives are not a register)
2. Absence of register of medical clinics with conditions for diagnosis and treatment of such diseases and specialists with enough experience in this area.
3. Insufficiency of quality and available information and scientific knowledge about rare diseases.
4. Limitation or absence of possibilities for diagnosis of the majority of rare diseases.
5. Difficulties in gaining access to treatment if it exists.
6. Absence of protocols of control of patients in the majority of the diseases.
7. Absence of education programs for doctors of polyclinics in rare diseases.
8. In absence of diagnosis, registration and protocols of control of patients there is no basis for appropriation of budgetary funds for their treatment.
9. Insufficiently effective and inadaptable system of drug assurance.
10. Absence of laws regulating situation with rare disease and drugs for their treatment.
11. Absence of working system of planning and adaptable monitoring of situation with rare diseases.
12. Incomplete mutual understanding, interaction and coordination in public authorities, medical and social workers and patients.
13. State doesn’t have enough “political will” for solution of this problem, civil servants don’t want to solve it, and patients don’t believe in change of situation.

These problems are not individual, they are shared problems for the majority of countries. Difference is in that in other countries these problems have been already started to be resolved, in Russia this problem doesn’t exist from the viewpoint of civil servants.

Part IV. Role of patient’s organizations in the solution of problem of patients with rare disorders

Patient with rare disease very often is face to face with his disease. His problem doesn’t interest society and authority and seems unessential against solution of global task. Therefore patient’s organizations play a great part in the handling of problems of patients with rare disease, because only their union may help to get something moving in this situation.

First national organization of patients with rare diseases was formed in USA in 1983 (National Organization for Rare Disorders – NORD). Founders of this organization were patients and their relatives initiating enactment and taking a part in the development of a law about rare diseases and orphan-drugs (Orphan Drug Act) in USA. The primary task of NORD is “identification, treatment and care of patients with rare disorders via realization of educational and research programs, upholding of their interests and rendering of a service”.

European organization of patients with rare diseases (EURODIS) was constituted in 1997. It is uncommercial, nongovernmental managed by patients association of organizations and people are around in area of rare disorders. Mission of Eurodis consists in creation of strong all-European community of organizations of patients with rare disorders, their self-expression at the European level, direct or indirect fight against influence of the disease on their life. Currently EURODIS unites more than 320 patient’s organizations from 19 European countries and includes 29 millions of patients in European Union.

There are singular patient’s organizations in Russia. Inactivity of patients is caused by their limited physical capacity and unbelief in possibility of influence on administrative state system and change of their life situation. At the present time only several organizations are around: All-Russia charitable public organization of invalids
“All-Russian society of hemophilia” (formed in 2000), Multiregional public organization “Care of patients with mucoviscidosis” (formed in 1997), Multiregional public organization of favor for persons disabled from childhood with Gaucher disease and their families (formed in 2000), All-Russia Public Organization of invalids – patients with multiple sclerosis (created in 2001), Multiregional charitable public organization “Society of invalids suffering from Hunter’s syndrome, other forms of mucopolysaccharidosis and another rare genetic diseases” (created in 2004), Charitable fund “Association of parents of children-invalids “Angel” (rare genetic diseases) (created in 2004), Non-profit organization “Northwest society of patients with rare disorders” (created in 2005).

Early in the 2008 year in St. Petersburg it was constituted National Association of organizations of patients with rare diseases “Genetics”. The main objective of Association is alliance of organizations of patients with rare disorders and rare genetic diseases throughout Russia. Main task is synchronization and coordination of work intending to improvement of health and social position of patients; help in organization of their treatment, socialization and rehabilitation; drawing of attention of public authority, local government and general public to existing problems of patients; preparation of suggestions in public authorities of Russia and subjects of the Russian Federation directing on development and perfection of legal framework, regulatory framework associating with handicapped children, their parents and other patients with rare diseases; distribution of information about rare disorders, modern facilities of their diagnosis and treatment; exhibition and protection of rights and legitimate interests of patients. In many regions of our country parents of sick children and patients themselves don’t know how to protect their rights, but taking support from Association they start to join for united actions.

Dialogue between government, patient’s organizations and medical services is difficult. Form of interrelation “civil servant – doctor – patient” is not usual for our society. Traditionally every person tries to solve his problem himself, alone, in accordance to his own understanding (often wrong) and viewing of issues, and what concerns civil servants – with least expense of energy, time and money. And if problem is not solved then it will be lost. Every person in this association has his own point of view is not understandable for other, his own thoughtway, own viewing of situation, his own “true”. For instance many doctors consider that patient shouldn’t be provided information about his disease. Some patients have similar opinion. To gain understanding and cooperation for pursuing a general goal we should learn to understand each other, but it requires time and desire.

Currently attempts of establishment of the connection have been already undertaken. In April 2007 Federal Service for the Supervision of Public Health and Social Development and some patient’s organizations related to group “7 nosologies” completed an agreement about interaction in aspects of the enhancement of drug assurance of people and information exchange.

In July 2007 minister of Public Health M. Zurabov had met with representatives of associations of patient’s societies: All-Russia society of hemophilia, multiregional public organization of invalids “St. Petersburg society of persons suffering from epilepsy”, public organization “St. Petersburg diabetic society of invalids”, All-
Russian public organization of invalids with multiple sclerosis, multiregional public organization “Favor for persons disabled from childhood with Gaucher disease and their families”, autonomic non-commercial organization on administration for patients with oncologic and oncohematologic diseases “Favor”, multiregional public organization of invalids “Rheumatologic association “Hope”. This meeting resulted in making decision about forming of constantly acting working group within Ministry, active partnership in the development of standards of treatment of these nosologies, actualization of a register of patients taking a drug therapy, participation of representatives of associations in tenders on purchase of drugs and also organization of rational logistics of the getting of drugs by patients.

January, 25 2008 the head of Federal Service for the Supervision of Public Health and Social Development Nikolaj Yurgel signed the Order “About forming of public councils within State Boards in Federal Service for the Supervision of Public Health and Social Development of subjects of Russian Federation” In accordance to words of professor Yurgel participation of patients and public associations in the discussion of problems in the reforming of healthcare system, improvement of the quality and availability of medical care, organization of control and supervision within the healthcare sphere is an important element of civil society. “To provide effective interaction of State authorities, business, local authorities and public associations it should be constant and based on principles of voluntariness, professionalism and openness. Only in this case we may reckon on creation of real effective and associated with patients interests systems of healthcare in our country” – said the head of Federal Service for the Supervision of Public Health and Social Development.

With enough active position of Ministry of Public Health and Social Development and Federal Service for the Supervision of Public Health and Social Development at the regional level there are big problems with forming of partnership. It deals with absence of regulating documents. Recently Committee of Public Health of St. Petersburg government give us an answer for our suggestion to complete an agreement about partnership with some organizations of patients: “Ministry of Public Health and Social Development “makes a decision” itself and we don’t have such seals.” But it should be noted that we haven’t ever been refused in help dealing with solution of problems in concrete patients. Similar situation was in Medico-genetic centre, where head geneticist of St. Petersburg forbade (didn’t recommend) to sign any agreements with patient’s organizations.

To avoid such problems it must be developed code of ethics in the work of patient’s organizations, defined legal status of organizations representing patient interests in interaction with executive authorities; solved the question of control by public organizations in drug market for making and directing of lists of patients in regions and at federal level etc.

There is also real need in forming of so called “schools of patients”, performing of special trainings to provide patient and his relatives with maximal volume of information about his disease, teach them to estimate really and to perceive current situation. Simply try to teach them to live newly within the fight and peace with their disorder. For many patients particularly for those who take an effective treatment it becomes a special lifestyle. And public organization must play the part in
this case. Lately such practice is widely spread in other countries and proves its high effectiveness. For example it becomes a good and useful tradition to hold of annual summer meetings of families of patients with mucopolysaccharidosis and other rare genetic diseases in Poland. But a trip aboard is not always possible because of physical and financial difficulties. It is time to think about creation of such “schools of the survival” in Russia.

Firstlings of partnership of state authorities, medical workers and patient’s organizations have been already got. This includes enrollment of drugs for treatment of rare diseases in federal program of additional pharmacologic support that leaded to real availability of drugs for the treatment of mucoviscidosis, hemophilia from 2005, Gaucher disease – from 2006. This is the beginning of the realization in 2008 of program “7 nosologies” (this program includes hemophilia, mucoviscidosis, Gaucher disease, multiple sclerosis – 4 from 7 nosologies). This is approval of Act of accelerated procedure of state registration of drugs.

Such facts show that situation may be changed and it must be changed. Patients suffering from rare disorders get a real hope.

People suffering from rare disease, let’s join together!

Part V. Very rare day for special people

February, 29 2008 became the first International Day of patients with rare disorders. Choice of this date for such action is not occasional. 29th day of February becomes once in 4 years and this is a symbol of rarity. On this day in many countries of the world (European Union, USA, Canada, Croatia, Ukraine, Armenia, Russia etc.) there were organized hundreds of actions dealing with problems of patients with rare disorders and causing great public resonance. Purpose of these actions was drawing of attention to problems of patients with rare disorders, increase of informational awareness about rare diseases and their influence on human lives, best understanding of their importance as priority of public healthcare.

Why was this day organized?
• Because there are children and adults with rare disorders and they need care
• Because it is necessary to spread the information about rare diseases in healthcare workers and population. Information is a basis for improvement of their life conditions;
• Because the day “is focused” on rare disorders may help to keep the hope for sick persons.
• Because financial support is required for the solution of social and medical problems of patients and performing of research investigations;
• Because simultaneous coordinated activity all over the world may guarantee that patients with rare disorders will be attended;
• Because coordination of activities at the national level and in the different regions is necessary;
• Because rare disorders must became a priority for the healthcare.
In Russia activities associating with International day of patients with rare diseases were held in Moscow and St. Petersburg.

In Moscow February, 28 2008 there was a press-conference in the informational agency “RIA-News” on a topic: “First European day of rare disorders”. Within press-conference it was manifested Note of Career Service in rare nosologies of Formulary committee of Russian Academy of Medical Sciences “Statement with drug assurance of patients with 7 rare expensive disorders at the end of February 2008”.

In St. Petersburg press-conference “Very rare day for special people” took place February, 26. It was organized by National Association of organizations of the patients with disorders “Genetics”. Representatives of public organizations of patients with rare diseases, doctors are specialized in diagnosis and treatment of such patients, patients with rare diseases and their relatives, representatives of companies manufacturing of orphan drugs, representatives of mass media took a part in this conference. It was organized an exposition of pictures and photo of children with rare diseases, off-site seminars in medical and educational institutions of the city. We should learn to make arrangement, find the way of the solution of problems because problems are numerous and are solved in fragmentary form.

Part VI. Personalized medicine and treatment of rare disorders as a strategic approach of the development of healthcare till 2020

Opened discussion of the Conception of the development of Russian healthcare till year of 2020 is certainly important and necessary step. A few years ago it was just a dream. However analysis of current suggestions and conceptions shows domination of estimates of present situation in healthcare and proposal of its solution. But real strategic planning with world-wide tendencies in the development of healthcare, medical and allied sciences and spheres is poor, but planning is for a long-term period – more than 10 years forward. Materials of site don’t include information about rare diseases although this direction is one of the 3 priority area of the development of healthcare in advanced countries during several years.

To our opinion priority of the conception should be presented by “assurance of real access to diagnosis, treatment and medical care” for all people particularly for patients with rare diseases.

As main strategic directions we suggest follows:
1. Improvement of knowledge in epidemiology of rare diseases.
2. Identification of the peculiarities of rare diseases.
3. Development of the information about rare diseases for patients, specialists in healthcare and society in total.
4. Education of specialists in healthcare for improvement of the diagnosis of rare diseases.
5. Organization of screening, improvement of diagnosis and assurance of its access
6. Facility of the access of patients to treatment and quality medical care.
8. Realization of specific wants of persons with rare disorders, perfection of rehabilitation system.
10. Creation of required infrastructure which provides precise coordinate work of all elements of healthcare system.
11. Development of national and international partnership in sphere of rare disorders.

For assurance of the realization directions being listed above we may mark next tactical tasks:

1. Analysis of situation with medical and social care of patients with rare diseases, Creation of operative computerized system of epidemiologic control for rare (and not only) disorders with accordance of their peculiarities and variety. The main element of this system should be presented by national register of patients with rare diseases, active register with inverse relationship with patient’s organizations and individual patients. This will allow combining current discrete databases, accumulating and analyzing incoming information for operative making administrative decisions and business-planning in associated with medicine innovative spheres of national economy. Significance of such system for medicine is similar to significance of building of road network for national economy of the country in total. In absence of the information about true occurrence of the disease it can’t be estimated need in some drug or method of treatment, it is difficult and often impossible to provide financial support for scientific investigations and commercialization of current developments.

2. Analysis, calculation and cost certification for the treatment and social rehabilitation of patients with rare diseases, estimation of its economic expediency.

3. Forming of system of monitoring of the realization of programs of drug assurance and medical care and analysis of its effectiveness.

4. Improvement of knowledge in rare diseases for best understanding of their coarse, estimation of requirements in resources and their rational usage, control of “progress” of patients within the healthcare system and estimation of treatment effectiveness.

5. Improvement of the informational awareness of the society, medical and social workers, patients and their relatives in rare disorders, modern possibilities of their diagnosis, therapy and rehabilitation of patients with rare diseases. Creation of Russian-language informational resources providing access to true and up-to-date information in this area in real time processing.

6. Support of organizations of patients with rare diseases. Enaction of legislative acts regulating interactions of organizations with medical and social services and state authorities.
7. Compilation of databases of medical and social institutes (and single specialists) with availability, experience in treatment and rehabilitation of patients with different rare disorders, where patients may be given a consultation and medical and social care.

8. Development and introduction of national protocols and standards of diagnosis, treatment and monitoring of rare diseases and conditions.


10. Enlargement and perfection of organization of screening programs in rare diseases (population screening: prenatal, neonatal, in adults; principal screening).

11. Increase of availability of diagnostic research by creation of new and/or improvement of current equipment of laboratories in federal districts and subjects of Russian Federation.

12. Making of networks in medical and medicosocial care for patients with rare diseases from consultative centers in subjects of RF\(^1\) with combined coordination of their work by major research institutes. Giving of expert seals for consultative centers. Providing of role of these centers as sources of information for patients and their families.

13. Forming of distinct departments in Ministry of Public health and control agencies of healthcare for organization of medical care of patients with rare disorders and operative solution of their problems, and working groups about special diseases including Ministry workers, physicians with experience in treatment of such patients and representatives of patient’s organizations.

14. Providing of coordination between state authorities, healthcare institutes, institutes of social care and education, manufacturers and suppliers of medical products and public organizations in sphere of state politics dealing with treatment and social care of patients with rare diseases by the formation of coordinate councils at the federal level and within subjects of RF.

15. Coordination and providing of governmental support of scientific researches of the diagnosis and treatment of rare diseases.

16. **Enaction of legislative package regulating activity in area of rare disorders and rare medical technologies.**

17. Partnership with international authorities: World Healthcare Organization, appropriate committees and commissions of European Union about the development of nomenclature and classification being adapting for rare diseases.

Of coarse these suggestions are draft copy of program and require careful discussion, study, estimation and add-in. But any new project has a starting point and then success of this project may be reached by stable and persistent work of all

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interested sides and objective groups. We hope that all abovementioned and suggested will be such starting point and help to make a progress in national healthcare system.

**Why personalized medicine, diagnosis and treatment of rare diseases must become one of the priority ways of the healthcare development in our country?**

1. Because development of such direction is a world-wide tendency. We came to the definite stage of social development when it appears a need to proceed from mass treatment to individual. Because all advanced states have already passed this reach.

2. Because new drugs and methods of treatment are developed for greater number of earlier incurable diseases and result in recovery of patient or feeling themselves as healthy and socially adapted persons.

3. Because early detection and therapy of rare disorder being started in time allows to economize big funds due to absence of necessity of expensive treatment at late stages of the diseases, decrease of expenses for alimentation and rehabilitation of patient, absence of perennial payments of disability grant, payments for disability to patient and his relatives. In many cases person may stay a full member of society, make himself useful with his work, create material, intellectual, cultural and other values.

4. Because according to act 41.1 of Constitution of Russian Federation “Every person has a right to health protection and medical care”…regardless of frequency of occurrence of his disease.

5. Because in accordance to act 17 of Fundamental principles of legislation of Russian Federation about health protection of subjects (Federal law from August, 22 2004, № 122-ФЗ) “State provides health protection of subjects independent from their sex, race, nationality, language, class origin, post, place of residence, religious commitment, creed, membership in public associations and other conditions. State guarantees protect of subjects from any form of discrimination is due to their diseases.”

6. Because this direction reflects basis of world view of Russian medical school being formed by S.P. Botkin.

7. Because rare diseases result in political problem: taking into account requirements of most delicate and small group of population. If we want to guarantee equal access to treatment and to reach the highest quality of care and support it is obvious that this problem requires change of healthcare system in total and medicosocial care.

8. Because development of approaches to diagnosis and treatment of rare diseases is one the main sources of innovations in medicine. Experience of producing of orphan drugs for treatment of rare diseases will allow to use developments in sphere of biotechnology, tissue and gene engineering for treatment of the majority of diseases including common disorders.

9. Because this direction may be growing-point, indicator of perfectibility and effectiveness of work of healthcare system.
10. Because it may be stimulus to development of native pharmaceutics, bio- and nanotechnologies, genetics and other spheres of national economy. In absence of this development it is difficult to organize effective system of introduction (commercialization) of innovative developments in medicine.

In respect of all factors rare diseases should become one of the priority directions of the development of native medicine at a period till year of 2020. **This direction certainly has a strategic, infrastructural and systemic significance.** Its development results in appearance of a good chance to reach obvious progress in health status and life expectancy in population to 2020 year. The most important aspect is not to avoid solution of problems and try to solve them orderly and hardly. And then result will be apparent.