

Tobacco smoking – popularity and main trends on research

Palenie tytoniu – rozpowszechnienie i główne kierunki badań

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ABSTRACT

Each year smoking leads to the premature death of over 5 million people around the world. However, the tobacco industry took actions like introducing cigarettes which contain less nicotine and tar aimed at not only maintaining the old clientele, but also attracting a new one. The knowledge of the adverse health effects of smoking became widespread in the second half of the 20th century and changed attitudes towards smoking. In recent years, in many markets in the world a new device representing an alternative to tobacco products was introduced. Electronic cigarettes are designed to deliver nicotine into the respiratory system in the form of an aerosol. They have been gaining more and more popularity, as evidenced by the increase in the percentage of users as well as in the numbers of publications about them. Currently, opinions are divided and the e-cigarette has almost as many supporters as opponents. All this resembles the situation concerning conventional cigarettes in the 20th century.

The aim of the study is to gather the most significant information concerning, on the one hand, the spreading popularity of tobacco smoking and, on the other, the research topics undertaken by contemporary scientists, as well as the government actions meant to protect from dangers of nicotine addiction in the 20th and 21st century. New developments of products containing this highly addictive substance call for systematic research in the interest of public health.

Key words: cigarettes, smoking, tobacco, electronic cigarettes

STRESZCZENIE

Palenie tytoniu jest przyczyną śmierci około 5 milionów ludzi rocznie na całym świecie. Wiedza na temat szkodliwego wpływu palenia na zdrowie stała się powszechna w drugiej połowie XX wieku. Jednak na prze-

strzeni lat przemysł tytoniowy podejmował działania mające na celu utrzymanie starych i pozyskanie nowych konsumentów. Jednym z nich było wprowadzenie na rynek papierosów o obniżonej zawartości nikotyny i substancji smolistych. W ostatnich latach na wielu światowych rynkach pojawiły się urządzenia zwane elektronicznymi papierosami. Zostały one zaprojektowane, jako produkt alternatywny do konwencjonalnych papierosów dostarczając nikotynę w formie aerozolu do organizmu użytkownika. Cieszą się one coraz większą popularnością, na co wskazuje wysoki odsetek ich użytkowników oraz ilość ukazujących się na ich temat publikacji. Obecnie zdania są podzielone i elektroniczne papierosy mają

wielu zwolenników jak i przeciwników. Przypomina to sytuację dotyczącą konwencjonalnych papierosów z XX wieku. W pracy zebrano najistotniejsze informacje na temat rozpowszechnienia palenia, jak i informacje na temat działań podejmowanych przez rządy oraz naukowców w celu ochrony zdrowia publicznego. Wiedza ta może być przydatna w nadchodzących latach ze względu na pojawiającą się szeroką gamę produktów takich jak elektroniczne papierosy, zawierających substancję uzależniającą, jaką stanowi nikotyna.

Słowa kluczowe: papierosy, palenie, tytoń, elektroniczne papierosy

INTRODUCTION

Nicotiana tabacum is indigenous plant for America and Australia [1]. That plant grew in America initially in the wild form of *Nicotiana rustica* and later in the cultivated form *Nicotiana tabacum* [2]. The plant and its properties were widely known by pre-Columbian civilizations. When the Spanish conquistadors arrived in the 15th century, they found among the Maya people in Yucatan rich traditional medicine [3]. According to Francisco Javier Clavijero, the Jesuit historian, the smoking habit was well known in pre-Columbian time and the Aztecs smoked tobacco after meals [4]. However, tobacco as such was introduced to Europe by Christopher Columbus. In the manuscripts of Columbus issued by Father Bartolomeo de Las Casas in 1514, we read that the native American people smoked leaves of the plant that Columbus received from them as a gift. This plant was *Nicotiana rustica*. The name tobacco comes from the fact that the Spaniards twisted the original name “tabacco”, which meant a tube or pipe for burning leaves of the plant [3]. In Europe tobacco smoking was also used primarily to treat illnesses such as headaches or stomach problems [5]. Similar properties of the plant were used by French ambassador in Lisbon Jean Nicot. The name of the plant and its main alkaloid came from his name [6]. The Europeans were responsible for the spread of the American habit of smoking to the rest of the world. During the 1600s, tobacco spread throughout Europe, and some Asian countries as well as the west coast of Africa. For example, in accordance with Japanese sources smoking pipes had been brought to Japan in 1600 with the English adventurer William Adams [7].

The earliest expression of opposition to smoking was the decree of King James I in 1604 year ban-

ning smoking [3]. James I of England was opposed to tobacco use and wrote the first major anti-tobacco treatise “Counterblast to Tobacco”, which also mentions the problem of passive smoking in 1604. The most famous paragraph says: “*a custome loathsome to the eye, hatefull to the Nose, harmful to the braine, dangerous to the lungs, and in the blacke stinking fume thereof, neerest resembling the horrible Stygian smoke of the pit that is bottomelesse*”. In spite of that paper, tobacco use increased. The king softened his position on tobacco use in order to collect the income from its taxation [8]. In 1634 in Russia Tsar Mikhail Fyodorovich banned tobacco smoking. This was attributed to the fire accident in Moscow caused by the cigarette. Similarly, in 1642, Pope Urban VII included in his bull the opposition to the habit of smoking. In the same year the Chinese emperor Chongzhen issued a decree banning smoking. A violation of this prohibition was supposed to be punished as severely as conspiring with the barbarians [3]. Despite the votes in favor of banning smoking and the harmful effects of tobacco, it was becoming more widespread. The greatest increase in its availability occurred in the 18th and 19th, when two innovations helped cigarette companies to popularize their products. Although the first tobacco advertisement in the United States ran in 1789 in New York newspaper [9], the advertising and packaging intensified in the late 1870s with the color lithography [10]. The second, introduced in the 1880s, was a cigarette-making machine that dramatically increased their production. A company could produce up to million cigarettes per day, instead of producing only thousands of hand-rolled cigarettes [11]. The expansion and increase of tobacco dependence among the public was also exacerbated the First and Second World War during which cigarettes were distributed to the soldiers with food rations

[12, 13]. Supposedly, sporadic reports on lung carcinoma were caused by the fact, that smoking was a rare habit to the 1920s [5]. Early toxicology studies on smoking should be traced back to the 19th century. One of the first papers pointing out tobacco and tobacco smoke contain certain chemicals occurred in 1828 [14], when Poselt et al. isolated the nicotine from tobacco – the substance responsible for addiction. Nonetheless, before the end of the 19th century the link between lung carcinoma and smoking was not suspected. This issue began to be taken into consideration in the early 1920s, when scientists started to investigate cigarette smoking as one of the explanations for more lung carcinoma cases [15]. The first studies on this phenomenon, failed to find evidence for health consequences of cigarette smoking. There were numerous theories implicating correlation between diseases and the exposure to tobacco smoke. Although they were focused on the effect of tobacco smoking on patients, the risk was difficult to confirm [16, 17]. The large-scale studies documenting the correlation between cigarette smoking and carcinoma appeared in the 1950s [18].

Subsequently, number of studies have demonstrated that cigarette smoking accounts for 30 percent of some carcinomas, including lung, mouth, throat, esophagus, bladder, kidney carcinoma and some leukemia. It was also shown that it could cause some heart and vascular diseases, chronic obstructive lung disease and other health problems [19]. In 1964 the U.S. Surgeon General, reported that cigarette smoking was most probably responsible for carcinoma of the lung and other health problems. These reports mark the beginning of modern public-health efforts to control tobacco use [5].

IMPORTANT FACTS AND SCIENTIFIC PAPERS ABOUT TOXICOLOGY OF TOBACCO

20th century

In the 1930s and 1940s smoking had become common in the United States among many physicians. The same happened in Europe, where for example in 1948 the percentage of smokers reached 45% [20]. The public and scientific anxiety about risk to health connected with smoking created concern among the tobacco industry. The companies began to include physicians as an iconic and reassuring figure in advertisements [21]. First works suggesting the relationship between smoking and carcinoma appeared in the late 1920s and 1930s. In 1928 Lombard and Doering [22] did not focus es-

pecially on smoking in relation to cancer, but on the general habits of people with cancer. They concluded that there is relation between “heavy smoking” and carcinoma. Two works that are engraved in the history of research on the toxicology of tobacco are papers by Roffo [23, 24] published in German. First from 1931 “Durch Tabak beim Kaninchen entwickeltes Carcinoma”, from the Journal *Zeitschrift für Krebsforschung* was one of the major works revealing a correlation between smoking and cancer risk [25]. The second work, “Krebs und Sarkom durch Ultraviolet- und Sonnenstrahlen”, from 1935, implicates that the tar from tobacco smoke causes the development of carcinoma after application on the rabbits’ skin [26]. However, this work received little popularity in the international scientific community, because of the allegation of cigarettes combustion in unrealistically high temperatures [27, 28].

The ground-breaking moment came in the year 1950, when several publications based on epidemiological studies conducted in the United Kingdom, the United States and Germany appeared. These were the first that kind of publications in English printed in reputable medical magazines [29–31]. In the *Journal of the American Medical Association*, Graham and Wynder [18] published their work showing the correlation between smoking and lung carcinoma. The study involved 684 patients with and 780 from control group without cancer and noted a statistically significant association between smoking and the occurrence of lung carcinoma. Within the study group as much as 91,2% were active cigarette smokers, 4% were waterpipe smokers, 3,5% were cigar smokers and 1,3% were non-smokers. Those results confirm that cigarette smoking is an important risk factor for lung carcinoma. In the same magazine a work showing the relationship between tobacco smoking and various types of carcinoma (lung, mouth, esophagus, trachea and colon) occurrence was published. The article of Levin et al. [32] “Cancer and Tobacco Smoking – A Preliminary Report” was based on a study involving 1045 men suffering from cancer and 605 men in the control group. The publication demonstrated that among smoking patients lung carcinoma occurs twice as often as among non-smoking patients. That study demonstrated the association between cigarettes smoking and the risk of mouth cancer. The publication of Norr “Cancer by the Carton” [33] appeared 1952 in publicly accessible *Reader’s Digest* to increase public awareness about the possible dangers of cigarette smoking. He highlighted the large rise in cigarette consumption in the United States

up to 2500 cigarettes per year for the average citizen of the United States. He quoted statistics of a 10 – fold increase in the number of deaths due to lung carcinoma in the U.S. between the years 1920–1948. Furthermore, from 1938 until 1948 that rate growth was about 144%. Norr referred to many scientific studies, including the previously described work of Wynder and Graham [18]. He noted the need of public awareness of the existing association between smoking and the risk of carcinoma. World discovery turned out to be another Graham's and Wynder's work [34]. Both scientists are considered to be pioneers of the research on the toxicity of tobacco. Their work was published in 1953 and clearly demonstrated that tar from tobacco smoke is responsible for cancer development. The study was carried out on mice. The scientists applied the extract from tobacco smoke to the skin of animals. The skin was examined twenty four month after application. It was shown that 60% of the animals had skin papilloma at the site of application. Simultaneously in the UK, the British Medical Journal published work in which it was shown that 100% of male and 68% of female patients with lung carcinoma were active smokers [31].

On 15th December 1953 the directors of the largest tobacco companies met with their lawyers and public relations specialists. The aim of that meeting was to develop strategies to minimize the losses associated with increasing scientific evidence concerning the risk connected with smoking. The result of this was the establishment of an “independent” research committee of the tobacco industry, designed to provide consumers with the impression that the tobacco industry took care of the health of smokers. The target was to show that independent investigation revealed no influence of smoking on health and that there was no evidence to show negative results from smoking as currently being published in the press. The most significant of these was the declaration sponsored by tobacco manufacturers and published in 1954 – “A Frank Statement to Cigarette Smokers”. The declaration appeared in 448 newspapers in the United States and was published in the form of advertising. It undermined the results of any studies proving that smoking causes cancer and by implication reassured consumers of its harmlessness [35, 36].

In the statement, we read:

“We accept an interest in people's health as a basic responsibility, paramount to every other consideration in our business.”

“We believe the products we make are not injurious to health.”

“We always have and always will cooperate with those whose task it is to Safeguard the public health.”

As a matter of fact, the agency did not achieve any significant results that could improve the health of smokers and today their actions seems to be focused on covering up the truth about the addictive and harmful effects of the cigarettes smoking. At this point the exchange of arguments began between the tobacco industry and those responsible for the protection of public health supported by scientists, who were active enemies of smoking. This was primarily concerned with changes in U.S. legislation and answers to these changes.

Three years after this event an official statement on smoking and health, saying that “Public Health Services feel the weight of evidence, which increasingly tend in one direction, which is that excessive cigarette smoking is one of the factors that cause lung cancer” was published [37, 38]. In 1957 Auerbach et al. [39] compared tissue sections from the bronchi of smokers in comparison to non-smokers. He found that basal cell hyperplasia and the microscopic changes were progressively more severe in the moderate and heavy smokers. In 1958 Hammond and Horn [40] analyzed the mortality rate of men in the USA and concluded that the death rate of regular cigarette smokers was 68% higher than that of a comparable group of men who had never smoked. In response to research the Federal Trade Commission proposed rules to regulate trade on cigarette labeling. It was made by control over the content and images in advertisements of cigarettes and by a ban on explicit or implicit health claims. Tobacco companies avoid these regulations by the establishment of a voluntary advertisement code about promotion of cigarettes in radio and television. After that the Public Health Service began transmitting the information to the public and claiming that there is no safe form of smoking [41]. Despite this fact, cigarettes still existed on television. They become inseparable attribute of celebrities, ranging from the history of Hollywood – Marilyn Monroe – ending with the stars of action movies. Sylvester Stallone for example, was paid half a million dollars to smoke Lucky Strikes in five of his “Rocky” and “Rambo” movies [18, 21].

In 1965 the increasing number of reports concerning the dangers of smoking led United States Congress to legislate the Federal Law about labeling and advertising tobacco products that replaced the federal, state and local regulations. As a result of that introduction there appeared warnings on cigarette packs: “Caution: Cigarette smoking may be

hazardous to health” [42]. In 1966 the Public Health Service submitted to Congress the “Technical Report on Tar and Nicotine”. Based on scientific evidence, it required hazardous ingredients such as tar and nicotine levels on labels and advertisements [41, 43]. Four years later United States Congress legislate a law banning cigarette advertising in radio and television, as well as requiring every cigarettes pack to carry a warning that cigarette smoking is harmful to health [44]. In 1971 the President of the United States Richard Nixon signed the National Cancer Act, providing donation on the research of cigarette smoking negative results on health [45]. In 1972 the United States Public Health Service classified several of identified chemical cigarette smoke components into various risk categories. The constituents categorized as the most hazardous were: tar, nicotine and carbon monoxide. It was suggested that lower level of those toxic substances in cigarettes smoke would reduce the negative results of smoking [46]. The report of the United States Public Health Service states that passive smokers are exposed to the harmful effects of tobacco smoke. The report quotes studies on animals, which proved detrimental effects of carbon monoxide on the structure and function of the heart and lungs. Thus the report suggested that carbon monoxide could cause a similar effect on humans [47]. In the middle 1970s, tobacco companies introduced cigarettes containing less nicotine and tar to the market [48]. In the 1970s Gori [49] performed research proving there were no negative results from smoking 1–2 cigarettes per day on smokers health compared to non-smokers. In 1978 Gori and Lynch [50] claimed that smoking 23 of one label cigarettes have no influence on the death rate. In the early 1980s, surveys of Kozlowski [51] and Benowitz [52] contested their hypothesis. Kozlowski claimed that smokers compensate for the lower nicotine content through deeper and more frequent puffs and clogging pores in the filters [51]. Benowitz et al. [52] published in *New England Journal of Medicine* results providing that “light” cigarette smokers do not receive lower doses of nicotine in comparison to smokers of “strong” cigarettes. Moreover the Surgeon General of the United States in the report entitled “The health consequences of involuntary smoking” emphasized that secondhand smoke leads to carcinoma of the lung in non-smoking adults, increases the risk of respiratory track diseases and impairs lung function in passive smokers [53]. The next report stated that the problem of smoking cessation is due to the addictive properties of nicotine [54]. Simultaneously with the study on smoking effects on

smokers’ health, the research started to focus on the impact of smoke on the people in the smokers’ environment. German scientist Lickint was the first who use the term “passive smoking” and pointed to the possibility of a relationship between exposure to tobacco smoke and the incidence of lung carcinoma [55]. The first publications about lung carcinoma among adult passive smokers were published in the early 80s. The first work pointing to the link between the risk of the incidence of lung carcinoma and exposure to tobacco smoke appeared in 1981. This has been shown on the basis of tests carried out on 91.000 women. The results of that survey shows that the risk of death due to lung carcinoma among non-smoking wives of smokers is twice in non-smoking women whose husbands also do not smoke [56]. In the same year appeared the other work confirming the findings of Hirayama [57]. In 1991 Glantz and Parmley [58] published in *Circulation* “Passive smoking and heart disease: Epidemiology, physiology and biochemistry” which confirmed that passive smoking also causes heart disease.

In 1995 the heads of the seven largest tobacco companies lodged a deposition in front of the U.S. Congress claiming that nicotine is not addictive. In subsequent processes, it turned out that they were aware of the nicotine addictive properties and in fact they undertook actions in order to spread tobacco smoking due to these properties [38]. They never stopped fighting to acquire new and retain old smokers. In 1998, tobacco companies signed an agreement named the Master Settlement Agreement, which defined the authorized advertising of tobacco products and required the payment of 206 billion dollars. That amount was compensation covering the medical expenses of active and passive smokers [59]. In the second half of the twentieth century, the percentage of smokers began to fall in some highly developed countries. In the UK, for example, the highest percentage of smokers in 1948 was 82 and 41%, respectively, for men and women [60]. The decrease in the percentage of smokers occurred in the years 1974 to 1994 and remained constant at 20% [61].

21st century

That trend certainly depended on generally spreading knowledge of the adverse health effects of smoking. Moreover, from 1997 to 2007 there has been a noticeable decrease in the percentage of smokers in developed countries including Japan, Germany and Norway, even though in many countries such as Greece it remains at the same level. In

Asia (including China) the percentage of smokers increased [62]. In recent years, a new device representing an alternative to tobacco products has been introduced in many markets in the world. The electronic devices called electronic cigarettes (e-cigarettes) or electronic nicotine delivery system (ENDS) are designed to deliver nicotine into the respiratory in the form of an aerosol. They were designed in China by pharmacist Hon Lik in 2003. Lik worked for Golden Dragon Holdings, which after the start of production of the device, changed its name to Ruyan (“like smoke”). It became the first brand of e-cigarettes, electronic device constructed of a system allowing the evaporation of a nicotine solution, battery, charger and interchangeable cartridges containing nicotine and other chemicals. E-cigarette with its appearance reminiscent of a conventional cigarette is designed to provide the body with nicotine at a dose similar to that contained in conventional cigarettes. Initially the area of sales included China, but later expanded into the United States, the United Kingdom and Australia [63].

The e-cigarette is a relatively new product and short time had passed since its entry into the market. In recent years specialized shops offering a wide range of these products have sprung up. Since 2005, in many highly developed and developing countries strong growth in the interest of e-cigarettes has been recorded. In the first years they were advertised and available primarily on Internet. Internet seems to play a very important role in promoting the product [64]. In the online survey of 1.347 participating in e-cigarettes from 33 countries, 41% of respondents said that they learned about e-cigarettes from Internet. Internet is the most important source of information about this product. Grana and Ling [65] during 2011–2012 examined trends in describing e-cigarettes on their brand websites. The claims with 95% percentage of popularity on e-cigarette websites were presenting e-cigarettes as healthier, cheaper and cleaner. Another widely made claim (88%) was the ability to use them anywhere and without creating secondhand smoke and so harmless to people around (76%). Information about its use and effectiveness in smoking cessation (64%) was also very common. Other research results were published in 2013 by Rooke and Amos [66]. Scientists analysed twelve newspapers in UK and Scotland and three popular news websites during 2007–2012. They got similar results to those obtained by the above mentioned authors. The biggest claim was that they are healthier than conventional cigarettes (71%) and that they can be used in smoke free areas (44%). Very common were also claims

about use by celebrities (41%). As much as 35 % first heard about this product from a friend and only 8 % saw another person use an e-cigarette [67]. The e-cigarettes presence in media and their promotion by celebrities are also significant. Many websites refer to famous people who use these devices. Some of them attach celebrities’ photos. Also television is cited as a source of e-cigarettes images. They seem also to lessen the image of the unpleasantness to non-smokers. This makes vaping something modern and stylish. For example they are used during the shows like interview of David Latherman with Katherine Heigl using e-cigarette [68]. The use of e-cigarette is also showed in movies for instance by Johnny Deep in the movie “The Tourist” [69].

Currently e-cigarettes are used widely. In the US in 2011 as much as 21% of smoking adults used e-cigarettes, which is double the percentage noted in 2010 [70]. With the increasing interest of potential consumers, e-cigarettes began to be a subject for research scientists. This is also due to the fact that there are still very few studies concerning its danger or safety. Currently, opinions are divided and the e-cigarette has almost as many supporters as well as opponents. On the basis of current knowledge, electronic cigarettes cannot be considered totally safe [71]. Studies published so far relate to the effects of using electronic cigarettes and their safety. However, because it is a new product still, there are no studies on their use in the long term. Electronic cigarettes are often advertised as potential substitutes for nicotine replacement therapy. The safety and effectiveness of these devices are difficult to estimate, due to their short time on the market. There is still relatively little research on their potential harmfulness or efficacy as NRT.

The medical community is worried that wide availability of e-cigarettes could increase worldwide nicotine dependence, especially among young people tempted by various flavor options offered in e-cigarettes. Vaping produce mist similar to smoke from burning tobacco. Because of that, the opponents of e-cigarettes are afraid of the situation that traditional smokers will substitute vaping for smoking without the intention of stopping smoking conventional cigarettes [71]. People currently smoking use e-cigarettes as a form of nicotine replacement therapy (NRT) to reduce the number of cigarettes smoked per day. And people who are ex-smokers used them in order to quit smoking habit [64, 72]. E-cigarettes were used by them as a potentially safer alternative to conventional smoking [73]. Polosa R. et al. [74] in 2011 published the results of the re-

search on the potential effectiveness of the use of e-cigarettes by smokers in order to support attempts to quit smoking. Participants in the study were tested 5 times: at baseline 4, 8, 12 and 24 weeks after the start. During each study, volunteers were asked about the product they use and how many cigarettes they smoke per day. They also measured the amount of carbon monoxide in exhaled air. The researchers obtained results showing that in 13 out of 40 participants after 24 weeks the use of e-cigarette the amount of cigarettes smoked per day decreased 50%. The average number of cigarettes smoked per day fell from 25 to 6 cigarettes per day ($p < 0.001$). And in 12.5 % of patients it decreased from 30 to 3 cigarettes per day ($p = 0.043$). The remaining 22.5% of patients stopped smoking, still using e-cigarettes.

Caponnetto et al. [75] reported similar reduction in cigarette smoking or abstinence after one year of using e-cigarettes by cigarette smokers and in schizophrenic smokers [76]. Pepper et al. [77] conducted a national online research among 228 male adolescents (ages 11–19) and indicated that <1% of those who tried e-cigarettes and 18% of those who never tried e-cigarettes, were willing to experiment with using them. And they have no preference whether the liquid is flavored or unflavored. Furthermore, the majority of the volunteers (67%) were aware of e-cigarettes. Choi et al. [78] demonstrated that smokers were more willing to experiment with e-cigarettes than non-smokers. However, another research on 11 groups involving 66 young adults (ages 18–26) showed that they favored e-cigarettes and other new tobacco products because of their various flavors. Goniewicz et al. [79] conducted a research among Polish students from 176 high schools (among students aged 15–19) and universities (among students aged 20–24) and indicated that 23.5% of high school students and of similar percentage of university students (19%) had tried e-cigarettes. But minority of all respondents (3.2%) who admitted trying e-cigarettes were non-smokers. The currently available evidence suggests that e-cigarettes vaping can be considered as a safer alternative to traditional smoking [80]. Manufacturers of these products, however, do not reveal the full composition of the substances contained in cartridges for these devices [81].

The Food and Drug Administration (FDA) informed the President of the Electronic Cigarette Association that the agency sent letters with warnings to five e-cigarettes' distributors for "violations of good manufacturing practices, making unsubstantiated drug claims, and using the devices as delivery

mechanisms for active pharmaceutical ingredients" [82]. In response to FDA concerns regarding e-cigarette use, Health New Zealand Ltd. (HNZ), private enterprise analyzed the safety of the Ruyan® e-cigarette. This research was supported financially by Ruyan®. In the research report it is recommended that smokers use the e-cigarettes as an alternative to conventional smoking [64]. Cahn and Siegel [83] published a paper supporting HNZ's recommendation. Scientists concluded that "electronic cigarettes show tremendous promise in the fight against tobacco-related morbidity and mortality."

The main ingredients found in e-cigarette cartridges and solutions include nicotine, propylene glycol, glycerin, and tobacco flavoring [84, 85]. Detailed toxicological characterization of the aerosol generated by e-cigarette by gas chromatography with mass detector (GC-MS) showed that the primary ingredients are water, propylene glycol (PG), glycerol, and nicotine [86]. PG, a solvent as approved by the FDA for use in foods is also the major ingredient of e-cigarette fluids which compose 90% of all solution [64]. PG is the main compound of e-cigarettes used to produce an aerosol. In the European Union, PG is an approved food additive. It is also often used as a humectant in cosmetics and medicinal products. So far, only a few studies on the potential health risks associated with inhaling glycol, happens in the case of e-cigarettes' use. According to these studies, propylene glycol inhalation may affect the respiratory system. Short-term exposure to propylene glycol in indoor air (309 mg/m³ per minute) causes irritation of the upper respiratory tract and eyes [87]. It was also proven that people in the theatre, who are often exposed to aerosol containing propylene glycol, are more susceptible to respiratory tract irritation [88].

Furthermore, inhalation of the PG increases the risk of acquiring asthma [89]. However, Laugesen et al. [90] in his report did not indicate any harmful effect of the e-cigarette aerosol in humans. Two research show nonconformity between the labeled nicotine content and the actual nicotine concentration in few brands of the e-cigarettes [91, 92]. Similarly, Hadwiger et al. [93] using high-performance liquid chromatography indicated nicotine content on products labeled as non-nicotine.

Investigations have shown that apart from the above-mentioned substances, some of hazardous compounds are also compounds in e-cigarette cartridges. Research conducted on 13 brands of e-cigarettes indicates the existence of carbonyl compounds in their aerosol. Only 4 out of 13 brands generated no carbonyl compounds, but the others

generated different types of them. The maximum concentrations of formaldehyde, acetaldehyde, acrolein, propanal, glyoxal and methylglyoxal were 260, 210, 73, 83, 42 and 38 mg/m³ respectively. Most notably were very high concentrations of formaldehyde, which in comparison for a typical cigarette smoking was 140 µg of formaldehyde/cigarette [94]. In addition the metabolite of acrolein was determined in the urine of e-cigarette users [95]. Laugesen [90] in the research supported by Ruyan[®] shows that tobacco-specific nitrosamines (TSNAs) are present, but their levels are much lower than in conventional cigarettes and too small to be carcinogenic. Williams et al. [96] found detectable levels of metals such as lead, chromium, and nickel in e-cigarette aerosol. They also found that these levels are equivalent to or higher than those reported in cigarette smoke. They indicated that the source of detected metals came from the filaments from the e-cigarette's cartomizer. They detected heavy metals and silicate particles in e-cigarette aerosol using techniques such as smoking machine, light and electron microscopy, article counter, x-ray microanalysis as well as cytotoxicity testing. Most of the abovementioned substances have been classified by the International Agency for Research on Cancer (IARC) as carcinogenic [97]. Because these substances are present in both aerosol and urine of users, it should be considered that the use of e-cigarettes increases the risk of carcinoma. In recent years research also focused on the potential impact of the substances contained in e-cigarette on a living organism.

Bahl et al. [98] conducted research concerning the effects of a different of e-cigarette refill fluids on human pulmonary fibroblasts (hPFs) and human embryonic stem cells (hESCs). He found that the nicotine content of e-cigarette refill fluids had no cytotoxic effect on both at any concentration. However, he found a positive correlation between the concentration and number of chemicals used as a flavor in e-cigarettes fluids and hESC cytotoxicity. Results published by Romagna et al. [99] indicated that an extract from e-cigarette vapour was less cytotoxic to cultured fibroblasts than an extract from conventional cigarette smoke. Flouris et al. [100] conducted determinations of white blood cell, lymphocyte and granulocyte count among active conventional cigarettes smokers but not among active e-cigarette smokers.

E-cigarettes seem to be safer than conventional cigarettes, but the available data seem to be insufficient to conclude that they are absolutely safe. Further studies are required for this assessment. An e-cigarette presents a topic for a global debate about

not only their safety, but also the legal regulations concerning them. There were no legal regulations concerning the quality of e-cigarettes throughout the European Union until 2014. The activities of numerous governmental and nongovernmental agencies were limited so far to the warnings about lack of sufficient research about their safety. Despite this type of statements, sales of e-cigarettes have increased notably in recent years. According to a survey commissioned by the European Commission in 2012, almost two-thirds (69%) of Europeans have heard of electronic cigarettes. As many as 46 % respondents also have quite wide knowledge about them [101]. Users of e-cigarettes are mainly young people, mostly men, who recently quit the smoking habit [64]. According to a study commissioned by Action on Smoking and Health (ASH), in 2010 only 3% of smokers used e-cigarettes. This number increased in 2012 to 7% and in 2013 it reached 11%. The percentage of people who have ever attempted to use the e-cigarette amounted to 9% in 2010 and increase up to 22% in 2012 and 35% in 2013 [102]. This leads to the newest regulations on e-cigarettes contained in Directive 2014/40/EU of the European Parliament and of the Council. In this paper for the first time the e-cigarette issue will be regulated, specifying exactly their status as tobacco products and the regulations concerning them. The European regulations on these fast developing devices come from the fact, that they differ in each Member State. The European Union imposes an obligation to report these products to the competent authorities in the Member State, giving detailed information of the manufacturer and importer. A detailed list of all substances in a product with particular reference to the effect of their inhalation on users' health will be required. Furthermore, there are strict regulations on nicotine-containing fluids used in electronic cigarettes. It must be marketed exclusively to the e-cigarettes with volume up to 10 ml. In the case of disposable cartridges the volume must be up to 2 ml and the concentration of nicotine in the liquid could not exceed 20 mg/ml. In addition, the directive prohibits the addition of the substances such as vitamins or others, which give impression that this tobacco product is beneficial to health and associated with the reduction of health risks. Furthermore, e-cigarettes and spare containers will have to be adequately protected against accidental opening by children. Individual package of e-cigarettes and spare containers will have to include a leaflet with instructions for products' use and storage. In addition, it will be required to include the information that the product is not intended for young people

and non-smokers. Other important information required on labels will be a list of all ingredients of the product sorted by decreasing weight and the exact concentration of nicotine in the liquid as well as in a single dose. Very important requirements concern health warnings on packages. This information must be placed on two major surfaces of package and occupy 30% of the surface. The regulations also apply to promotion of e-cigarettes. There will be total ban on the promotion and advertising of electronic cigarettes and their components. The new regulations come into force on 20 May 2016 [103].

CONCLUSIONS

The 19th and 20th century and the development of tobacco industry, wars and advertisement campaigns led to increase in number of smokers worldwide. Accumulated information indicates that with the higher proportion of smokers resulted in occurrence of more cases of certain diseases, especially lung carcinoma. These led the scientists to begin research on the existence of a correlation between smoking and the risk of lung carcinoma. In the 1950s this began to appear in the first study on this issue. More works demonstrating the harmful effects of smoking were published in the following years with the development of science. However, the tobacco industry undertook actions aimed at the popularization of tobacco products and retaining existing smokers. Today cigarette smoking is the cause of 80–90% of all lung carcinoma deaths and also increases the risk of other cancers, cardiovascular disease, lung disease and infectious diseases [104].

The number of deaths caused by the tobacco smoking is estimated to be 5 million each year and still increasing. Despite extensive preventive actions organized and strengthening anti-smoking law it is still a major problem in societies all over the world, [105] which should not be neglected.

At the beginning of the 21st century, as an alternative to tobacco products, the new device called electronic cigarettes were introduced. They were designed to deliver nicotine into the respiratory tract and imitate the conventional cigarette. They have gained more and more popularity since the first years of their sale. This fact is evidenced by the increase in the percentage of users. In the United Kingdom in 2010 there were 3% of e-cigarette users and in 2012 the amount rose to 11%. With the increasing interest of potential consumers, e-cigarettes became the subject of scientific research. This is due to the fact that there are still very few studies indicating unequivocally their harmfulness or otherwise. Currently, the voices are divided, and the e-cigarettes have almost as many supporters as opponents. All this resembles the situation concerning cigarettes in the mid-twentieth century and this requires further research on the use of e-cigarettes and their effect on their users' health. The industry connected with e-cigarettes has undertaken actions, especially advertisements of the product, which resemble the tobacco industry strategy of the 1960s. However, there are conclusions drawn from previous experiences related to the tobacco industry. Recent regulations for e-cigarettes appeared in the new Tobacco Product Directive from April 2014. These provisions appeared very quickly in response to their growing popularity, considering the fact that they appeared on the market only recently and started to be avail-

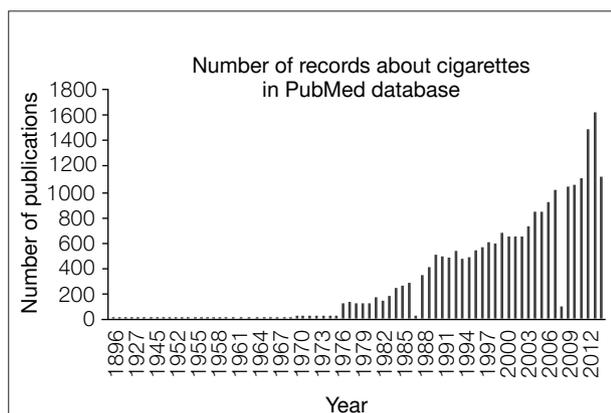


Fig. 1. Number of records on cigarettes in PubMed database per year

Ryc. 1. Liczba publikacji dotyczących papierosów ukazujących się każdego roku w bazie PubMed

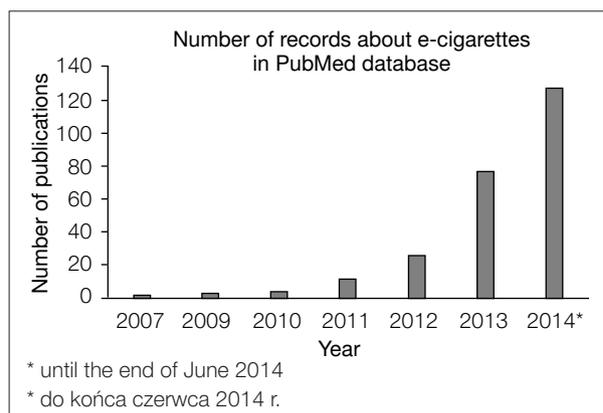


Fig. 2. Number of records on e-cigarettes in PubMed database per year

Ryc. 2. Liczba publikacji dotyczących e-papierosów ukazujących się każdego roku w bazie PubMed

able worldwide only since 2007. It seems to be an even faster response if we take into consideration the time of introducing identical legal provisions in the case of conventional cigarettes. They appeared in the 1960s, while the largest increase in their popularity was in the 1930s.

On the basis of current knowledge, electronic cigarettes cannot be considered as completely safe. There is still insufficient number of studies related to the effects of using electronic cigarettes and their safety published. There are no studies on their use in the long term, because they are a relatively new product. However the scientific community believes that e-cigarettes would be a health benefit if the population of conventional cigarettes smokers switched to this device. However, there is also a possibility that the promotion of safer alternatives to cigarette could inhibit smoking cessation among smokers, or that this product could be attractive to non-smokers. The other concern is about possible usage of this product by young people [106]. At this point we have to ask if the negative experiences of the last 50 years of the fight with tobacco industry could overshadow the health benefits for users who switch to e-cigarettes?

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REFERENCES

1. Feinhandler S, Fleming H, Monahan J: Pre-Columbian tobaccos in the Pacific. *Economic Botany* 1979; 33: 213-26.
2. Gately I: Tobacco: The Story of how Tobacco Seduced the World. Grove/Atlantic, Incorporated 2001.
3. Gilman S: Smoke: A Global History of Smoking. 2004.
4. Brooks J. E.: The mighty leaf: Tobacco through the centuries. Boston: Little, Brown and Company, 1953. *Science Education* 1954; 38(3): 245-245.
5. Benowitz N., Alice B., Homburg et al.: "Tobacco: History of." *Encyclopedia of Drugs, Alcohol, and Addictive Behavior*. 2004 [cited 2013 29.11.2013]; Available from: <http://www.encyclopedia.com/doc/1G2-3403100446.html>.
6. Monardes N.: Joyfull Newes out of the New Found World 1596.
7. Suzuki B.: The First English Pipe Smoker in Japan; William Adams, the Pilot and the English Trade House in Hirato 1600-1621, 1997.
8. Milne I.: A counterblaste to tobacco: King James's anti-smoking tract of 1616. *The Journal of the Royal College of Physicians of Edinburgh* 2011.
9. Petrone G.: Tobacco Advertising: The Great Seduction. Schiffer Publishing, Limited 1996.
10. Garfinkel L.: Trends in Cigarette Smoking in the United States. *Preventive Medicine* 1997; 26(4): 447-450.
11. Roberts B.: Inventions in the tobacco industry. 2006 [cited 2013 25.05.2013]; Available from: <http://www.learnnc.org/lp/editions/nchist-newsouth/4402>.
12. Hess H.: The other prohibition: The cigarette crisis in post-war Germany. *Crime, Law and Social Change* 1996; 25(1): 43-61.
13. Wootten H.: WOOTEN REPORTS 1940-1945. 1941: Printers' Ink Monthly.
14. Posselt W, Reimann L.: Chemische Untersuchungen des Tabaks und Darstellung des eigenhumlichen wirksamen Principles dieser Pflanze. *Geigers Magazin der Pharmazie* 1828; 24: 138-61.
15. Roffo A.: Was Man von dem Krebs wissen muss. *Aufklärungsschrift [What you should know about cancer: A popular exposition]*. Instituto de Medicine Experimental: Buenos Aires 1928.
16. Brandt A.: Cigarette Century: the Rise, Fall and Deadly Persistence of the Product that Defined America. *Tob Control* 2007; 16(5): 360-360.
17. Glantz S, et al.: *The Cigarette Papers*. Berkeley: University of California Press 1996.
18. Wynder E, Graham E.: Tobacco smoking as a possible etiologic factor in bronchiogenic carcinoma; a study of 684 proved cases. *J Am Med Assoc* 1950; 143(4): 329-36.
19. IARC Globocan 2008. *Cancer Fact Sheet: Lung Cancer Mortality Worldwide in 2008*. 2011 [cited 2013 29.11.2013]; Available from: <http://globocan.iarc.fr/factsheets/cancers/lung.asp>.
20. Snegireff L, Lombard O.: Survey of Smoking Habits of Massachusetts Physicians. *New England Journal of Medicine* 1954; 250(24): 1042-1045.
21. Gardner M., Brandt A.: The Doctors' Choice Is America's Choice. *American Journal of Public Health* 2006; 96(2): 222-232.
22. Lombard H, Doering C.: *Cancer Studies in Massachusetts: Habits, Characteristics and Environment of Individuals with and without Cancer*. New England Journal of Medicine 1928; 198(10): 481-487.
23. Proctor R, Angel H.: Roffo: the forgotten father of experimental tobacco carcinogenesis. *Bulletin of the World Health Organization* 2006; 84: 494-496.
24. Cooter R.: The Nazi War on Cancer. *BMJ* 2000; 320(7236): 721.
25. Roffo A.: Durch Tabak beim Kaninchen entwickeltes Carcinom. *Zeitschrift für Krebsforschung* 1931; 33(1-2): 321-332.
26. Roffo A.: Krebs und Sarkom durch Ultraviolett- und Sonnenstrahlen. *Zeitschrift für Krebsforschung* 1935; 41(1): 448-467.
27. Doll S.: Commentary: Lung cancer and tobacco consumption. *International Journal of Epidemiology* 2001; 30(1): 30-31.
28. Hanmer H, to Hahn P.: Memorandum on alleged causative relation between cigarette smoke and bronchiogenic carcinoma. 1950; available from: <http://tobaccodocuments.org/tplp.html>; accessed: 29.11.2013
29. Schrek R. et al.: Tobacco Smoking as an Etiologic Factor in Disease. I. Cancer. *Cancer Res* 1950; 10(1): 49-58.
30. Mills C.A., Porter M.: Tobacco Smoking Habits and Cancer of the Mouth and Respiratory System. *Cancer Res* 1950; 10(9): 539-542.
31. Doll R, Hill A.: Smoking and carcinoma of the lung; preliminary report. *Br Med J* 1950; 2(4682): 739-48.
32. Levin M., Goldstein H, Gerhardt P.: Cancer and tobacco smoking: A preliminary report. *J Am Med Assoc* 1950; 143(4): 336-338.

33. Norr R, Christian H.: Cancer by the carton. *Reader's Digest*, 1952 (12).
34. Wynder E, Graham E, Croninger A.: Experimental Production of Carcinoma with Cigarette Tar. *Cancer Res* 1953; 13(12): 855-864.
35. Tobacco Industry Research Committee, A frank Statement to cigarette smokers. 1954. available from: <http://tobaccodocuments.org.tplp.html>; accessed: 29.11.2013
36. Cummings K, Morley C, Hyland A.: Failed promises of the cigarette industry and its effect on consumer misperceptions about the health risks of smoking. *Tob Control* 2002; 11(suppl 1): i110-i117.
37. Burney L.: Excessive cigarette smoking. *Public Health Rep* 1957; 72(9): 786-786
38. Glantz S, Balbach E.: Tobacco war inside the California battles. 2000; available from: <http://search.ebscohost.com/login.aspx?direct=true&scope=site&db=nlebk&db=nlabk&AN=65741>; accessed: 29.11.2013
39. Auerbach O. et al.: Changes in the Bronchial Epithelium in Relation to Smoking and Cancer of the Lung. *New England Journal of Medicine* 1957; 256(3): 97-104.
40. Hammond E, Horn D.: Smoking and death rates; report on forty-four months of follow-up of 187,783 men. I. Total mortality. *J Am Med Assoc* 1958; 166(10): 1159-72.
41. Smoking and Health: Report of the Advisory Committee to the Surgeon General of the Public Health Service, E. United States Department of Health, and Welfare, Editor: Washington: US Department of Health, Education, and Welfare, Public Health Service 1964.
42. Cigarette Labeling and Advertising Act. U.S. Congress 1965.
43. United States, Reviewing progress made toward the development and marketing of a less hazardous cigarette: hearings before the Consumer Subcommittee of the Committee on Commerce, United States Senate, Ninetieth Congress, first session. August 23, 24, and 25, 1967. Washington, D.C.: U.S. Government Printing Office 1968.
44. Calfee J.: Cigarette Advertising, Health Information and Regulation before 1970. Bureau of Economics, Federal Trade Commission 1985.
45. Rettig R.: Cancer crusade: the story of the National cancer act of 1971. Princeton, N.J.: Princeton University Press 1977.
46. Holbrook J.: The changing cigarette. *West J Med* 1981; 134(4): 353.
47. The health consequences of smoking. Report of the United States Public Health Service. United States Public Health Service Washington 1972.
48. Institute N, The FTC cigarette test method for determining tar, nicotine, and carbon monoxide yields of U.S. cigarettes: report of the NCI expert committee. U.S. Dept. of Health and Human Services, Public Health Service, National Institutes of Health 1996.
49. Gori G.: Low-risk cigarettes: a prescription. *Science* 1976; 194(4271): 1243-6.
50. Gori G, Lynch C.: Toward less hazardous cigarettes. *Current advances. JAMA* 1978; 240(12): 1255-9. 51.
51. Kozlowski L. et al.: The misuse of 'less-hazardous' cigarettes and its detection: hole-blocking of ventilated filters. *American Journal of Public Health* 1980; 70(11): 1202-1203. 52
52. Benowitz N, et al., Smokers of Low-Yield Cigarettes Do Not Consume Less Nicotine. *New England Journal of Medicine* 1983; 309(3): 139-142.
53. Office on smoking and health. The health consequences of involuntary smoking: a report of the Surgeon General 1986: Rockville, Maryland: Public Health Service.
54. Office on Smoking and Health. The Health Consequences of Smoking: Nicotine Addiction: a report of the Surgeon General 1988.
55. Lickint F.: Bronchial carcinoma in non-smokers. *Munch Med Wochenschr*. 1954.
56. Hirayama T.: Non-smoking wives of heavy smokers have a higher risk of lung cancer: A study from Japan. *BMJ* 1981; 282: 183-185.
57. Trichopoulos D, Kalandidi A., Sparos L, MacMahon B.: Lung cancer and passive smoking. *Int J Cancer* 1981; 27: 1-4.
58. Glantz S, Parmley W.: Passive smoking and heart disease. *Epidemiology, physiology, and biochemistry. Circulation*, 1991; 83(1): 1-12.
59. Master Settlement Agreement. 1998; Available at: <http://publichealthlawcenter.org/sites/default/files/resources/master-settlement-agreement.pdf>; accessed: 29.11.2013.
60. Wald N, Nicolaides-Bouman A.: UK Smoking Statistics. 2nd edition, Oxford University Press 1991.
61. Opinions and Lifestyle Survey, Smoking habits amongst adults, 2012. ONS, Sept. 2013; <http://www.ons.gov.uk>; accessed: 29.11.2013.
62. <http://epianalysis.wordpress.com/2011/11/14/tobaccosales/>; accessed: 29.11.2013.
63. Caponnetto P., Campagna D, Papale G. et al.: The emerging phenomenon of electronic cigarettes. *Expert Rev Respir Med*. 2012 Feb; 6(1): 63-74.
64. Etter J.: Electronic cigarettes: a survey of users. *BMC Public Health*. 2010 May 4; 10: 231. doi: 10.1186/1471-2458-10-231.
65. Grana R, Ling P.: Smoking revolution: a content analysis of electronic cigarette retail websites. *Am J Prev Med* 2014 Apr; 46(4): 395-403.
66. Rooke C, Amos A.: News media representations of electronic cigarettes: an analysis of newspaper coverage in the UK and Scotland. *Tob Control* 2013.
67. Dawkins L, Turner J, Roberts A. et al.: Vaping' profiles and preferences: an online survey of electronic cigarette users. *Addiction* 2013 Jun; 108 (6): 1115-25.
68. Grana R, Ling P.: Smoking revolution: a content analysis of electronic cigarette retail websites. *Am J Prev Med* 2014 Apr; 46(4): 395-403.
69. Grana R, Glantz S, Ling P.: Electronic nicotine delivery systems in the hands of Hollywood. *Tob Control* 2011; 20(6): 425-426.
70. (CDC), C.f.D.C.a.P., CDC Newsroom, About one in five US adult cigarettes smokers have tried an electronic cigarette. 2013.
71. Council on Science and Public Health (CSAPH), A.M.A., Use of electronic cigarettes in smoking cessation programs. Report 6 (A-10), 159th Annual Meeting.
72. Foulds J, Veldheer S.: Commentary on Etter & Bullen (2011): could E-cigs become the ultimate nicotine maintenance device? *Addiction* 2011; 106(11): 2029-30.
73. Barbeau A., Burda J., Siegel M.: Perceived efficacy of e-cigarettes versus nicotine replacement therapy among successful e-cigarette users: a qualitative approach. *Addict Sci Clin Pract* 2013; 8(1): 5.
74. Polosa R. et al.: Effect of an electronic nicotine delivery device (e-Cigarette) on smoking reduction and cessation: a prospective 6-month pilot study. *BMC Public Health* 2011; 11: 786.
75. Caponnetto P. et al.: Efficiency and Safety of an eElectronic cigarette (ECLAT) as tobacco cigarettes substitute: a prospective 12-month randomized control design study. *PLoS One* 2013; 8(6): e66317.

76. Caponnetto P. et al.: Impact of an electronic cigarette on smoking reduction and cessation in schizophrenic smokers: a prospective 12-month pilot study. *Int J Environ Res Public Health* 2013; 10(2): 446-61.
77. Pepper J.K., et al.: Adolescent males' awareness of and willingness to try electronic cigarettes. *J Adolesc Health* 2013; 52(2): 144-50.
78. Choi K. et al.: Young adults' favorable perceptions of snus, dissolvable tobacco products, and electronic cigarettes: findings from a focus group study. *Am J Public Health* 2012; 102(11): 2088-93.
79. Goniewicz M., Zielinska-Danch W.: Electronic cigarette use among teenagers and young adults in Poland. *Pediatrics* 2012; 130(4): e879-85.
80. Trehy M., Ye W., Hadwiger M. et al.: Analysis of electronic cigarette cartridges, refill solutions and smoke for nicotine and nicotine related impurities. *Journal of Liquid Chromatography & Related Technologies* 2011; 34: 1442-1458.
81. World Health Organization (WHO). WHO Study Group on Tobacco Product Regulation report on the scientific basis of tobacco product regulation WHO Technical Report Series 955. WHO, Geneva 2009.
82. Woodcock J.: Letter to Mr. Matt Salmon President, Electronic Cigarette Association 2013. Available at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/UCM225263.pdf>, accessed: 29.11.2013.
83. Cahn Z., Siegel M.: Electronic cigarettes as a harm reduction strategy for tobacco control: a step forward or a repeat of past mistakes? *Public Health Policy* 2011; 32: 16-31. doi:10.1057/jphp.2010.41
84. Cobb N., Abrams D., E-cigarette or drug-delivery device? Regulating novel nicotine products. *N Engl J Med* 2011; 365: 193-5. 85.
85. Westenberger B.: Evaluation of e-Cigarettes. St. Louis, MO: Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research, Division of Pharmaceutical Analysis 2009. Available at: <http://www.fda.gov/downloads/drugs/Scienresearch/UCM173250.pdf>; accessed: 7.05.2014.
86. US Food and Drug Administration: Final Report on FDA Analyses 2009 <http://www.fda.gov/downloads/Drugs/ScienceResearch/UCM173250.pdf>.
87. Wieslander G., Norback D., Lindgren T.: Experimental exposure to propylene glycol mist in aviation emergency training: acute ocular and respiratory effects. *Occup Environ Med* 2001; 58: 649-655
88. Moline J., Golden A., Highland J. et al., Health effects evaluation of theatrical smoke, haze and pyrotechnics Report to Equity-League Pension and Health Trust Funds. 2000
89. Choi H., Schmidbauer N., Sundell J. et al.: Common household chemicals and the allergy risks in pre-school age children. *PLoS One* 2010; 5: e13423. doi:10.1371/journal.pone.0013423.
90. Laugesen M.: Safety report on the Ruyan® e-cigarette cartridge and inhaled aerosol. Edited by Health New Zealand Ltd. 2008. www.healthnz.co.nz; accessed: 29.11.2013.
91. Goniewicz M.L., Kuma T., Gawron M. et al.: Nicotine levels in electronic cigarettes. *Nicotine Tob Res* 2013; 15: 15866.
92. Cameron J., Howell D., White J. et al.: Variable and potentially fatal amounts of nicotine in e-cigarette nicotine solutions. *Tob Control* 2013. doi:10.1136/tobaccocontrol-2012-050604
93. Hadwiger M., Trehy M., Ye W. et al.: Identification of amino in electronic cigarette products using high pressure liquid chromatography with diode array and tandem mass spectrometric detection. *J Chromatogr A* 2010; 1217: 7547-55.
94. Uchiyama, S., Ohta K., Inaba Y. et al.: Determination of carbonyl compounds generated from the E-cigarette using coupled silica cartridges impregnated with hydroquinone and 2,4-dinitrophenylhydrazine, followed by high-performance liquid chromatography. *Anal Sci* 2013; 29(12): 1219-22.
95. Goniewicz M.L., Knysak J., Kosmider L. et al.: Assessment of electronic cigarettes as a source of exposure to acrolein. Presentation at the Society for Research on Nicotine and Tobacco (SRNT) conference, March 2013, Boston.
96. Williams M., Villarreal A., Bozhilov K. et al.: Metal and silicate particles including nanoparticles are present in electronic cigarette cartomizer fluid and aerosol. *PLoS One* 2013; 8: 3.
97. International Agency for Research on Cancer (IARC) (2013) Agents classified by the IARC monographs, Volumes 1-107. Last update on 4 October 2013, <http://monographs.iarc.fr/ENG/Classification/index.php>
98. Bahl V., Lin S., Xu N. et al.: Comparison of electronic cigarette refill fluid cytotoxicity using embryonic and adult models. *Reprod Toxicol* 2012; 34: 529-37.
99. Romagna G., Alliffranchini E., Bocchietto E. et al.: Cytotoxicity evaluation of electronic cigarette vapor extract on cultured mammalian fibroblasts (Clear Stream-LIFE): comparison with tobacco cigarette smoke extract. *Inhal Toxicol* 2013; 25: 354-61.
100. Flouris A., Poulianiti K., Chorti A. et al.: Acute effects of electronic and tobacco cigarette smoking on complete blood count. *Food Chem Toxicol* 2012; 50: 36003.
101. TNS Opinion & Social. Attitudes of Europeans towards Tobacco. Special Eurobarometer 385, Wave EB77.1 commissioned by the Directorate General Health and Consumers of the European Commission, Brussels; 2012.
102. Dockrell M., Morrison, R., Bauld, L. et al.: E-cigarettes: prevalence and attitudes in Great Britain. *Nicotine Tob Res* 2013.
103. Tobacco Products Directive (2014/40/EU) http://ec.europa.eu/health/tobacco/products/revision/index_en.htm#19
104. Office of the Surgeon General (US); Office on Smoking and Health (US). The Health Consequences of Smoking: A Report of the Surgeon General. Atlanta (GA): Centers for Disease Control and Prevention (US); 2004. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK44695/> accessed: 6.07.2014.
105. WHO report on the global tobacco epidemic, 2008: The MPOWER package. *Population and Development Review* 2008; 34(3): 581-581.
106. Benowitz N.: Emerging nicotine delivery products. Implications for public health. *Ann Am Thorac Soc* 2014; 11(2): 231-5.

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