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THE INFLUENCE OF INDUSTRY 4.0 IN PHARMACY AND PHARMA 4.0 CONCEPT

Radoje Jevtić [60]; Jovan Ničković[61]; Dragan Vučković [62]; Momčilo Ranđelović [63]; Jugoslav Đorđević[64]

Abstract

As an especially important part of the chemical industry, the pharmacy industry provides the production of pharmacy resources, medicaments, and a lot of other things that serve human health protection. The importance of this kind of industry is crucial for human health and, related to that fact; products of this industry are under strict and detailed national and international regulations. The quality system must be established and functioning at an exceedingly high level. That demands strict, detailed, and precise synchronization of many production processes and procedures with principles from production practice. As can be seen, there are almost unlimited fields for appliances of modern technologies that Industry 4.0 brings to the service of humans and human health. Realized changes are so great that future functioning cannot be imagined without basic principles of Industry 4.0, such as real-time monitoring, smart factories, smart manufacturing, medicament robotization production, the influence of the Internet of Things, etc. All of the notes have brought a new concept in pharmacy - the Pharma 4.0 concept. This paper was written to show the influence of Industry 4.0 in the pharmacy field, achieved benefits, innovative solutions, different smart manufacturing, transferring and storing of huge amounts of data, and data integrity and quality management in the form of one total new principle and concept - Pharma 4.0.

Keywords: *human`s health, industry 4.0, pharmacy, Pharma 4.0*

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THE HISTORY CONCEPT OF PHARMA 4.0

At the first degree of industrial manufacturing (model industry 1.0) related to the pharmaceutical industry, resources were strictly mechanics. The classic informational system didn't exist. Complete manufacturing was based on individual work. The organization level of the manufacturing, processes, and similar was at the level of craft shop and to adaptive behavior (Pharma 1.0). The next degree of industrial manufacturing (model industry 2.0) related to the pharmaceutical industry purported electrical resources. The manufacturing processes were developed and under constant improvement. The organization level of the manufacturing, processes, and similar was at the level of the base principles of scientific management and the beginning of using science for industrial and manufacturing management (Pharma 2.0). The next degree of industrial manufacturing (model industry 3.0) related to the pharmaceutical industry purported digitalization and computerization. The main characteristics of this degree were connection with stable behavior (Pharma 3.0). Automatization also has appeared. Complete new degree purported new method of organization and realization. The most important thing is the visibility and transparency of data (Pharma 4.0). Complete new approach purported predictive behavior, with all necessary possibilities of adoption. Modern new technologies, the first-place virtual reality (VR), augmented reality (AR), Internet of things (IoT), and artificial intelligence (AI) present a base for complete transfer to the Pharma 4.0 concept [1, 2].

The Organisation Concept of Pharma 4.0

Industry 4.0 had a great influence in many society and industry spheres. One of these spheres is Pharmacy. The influence of Industry 4.0 was and is so enormous that the new term for pharmacy can be adopted-Pharma 4.0. Essentially, the terms Industry 4.0 and Pharma 4.0 are the same. Every production organization in Pharmacy must: plan and track orders in real-time; manage materials supplies and pharmacy production resources; realize online quality research; realize online resources and materials research; realize online management of pharmacy plants; on-line tracking of different and enormous data and their management etc. Terms such as digital pharmaceutical manufacturing, Pharma 4.0, smart pharmaceutical manufacturing, intelligent pharmaceutical manufacturing, and similar today present the same concept. It is obvious that in many different spheres, so as in the Pharmacy, separate automatic processes, procedures, robots, machines, computers, and similar are integrated into the unique digital system of the pharmaceutical industry.

This system is managed with artificial intelligence (AI) techniques, principles and methods. New systems can be presented and observed as modern cyber-physical systems (CPS), with the presence of the Internet of Things (IoT), machine learning (ML), and cloud computing (CC). These systems are capable of multiple production and increase the quality of the products with very few bad effects, almost negligible, such as scrap production, losses, and similar. Modern ways of connections and networking provide real-time tracking and monitoring of all aspects and elements of manufacturing. The speed and efficiency of testing, examination, and obtaining results is almost unimaginable in comparison with the same speed a few years ago. The main concept of Industry 4.0 in the pharmaceutical industry is presented in Figure 1.

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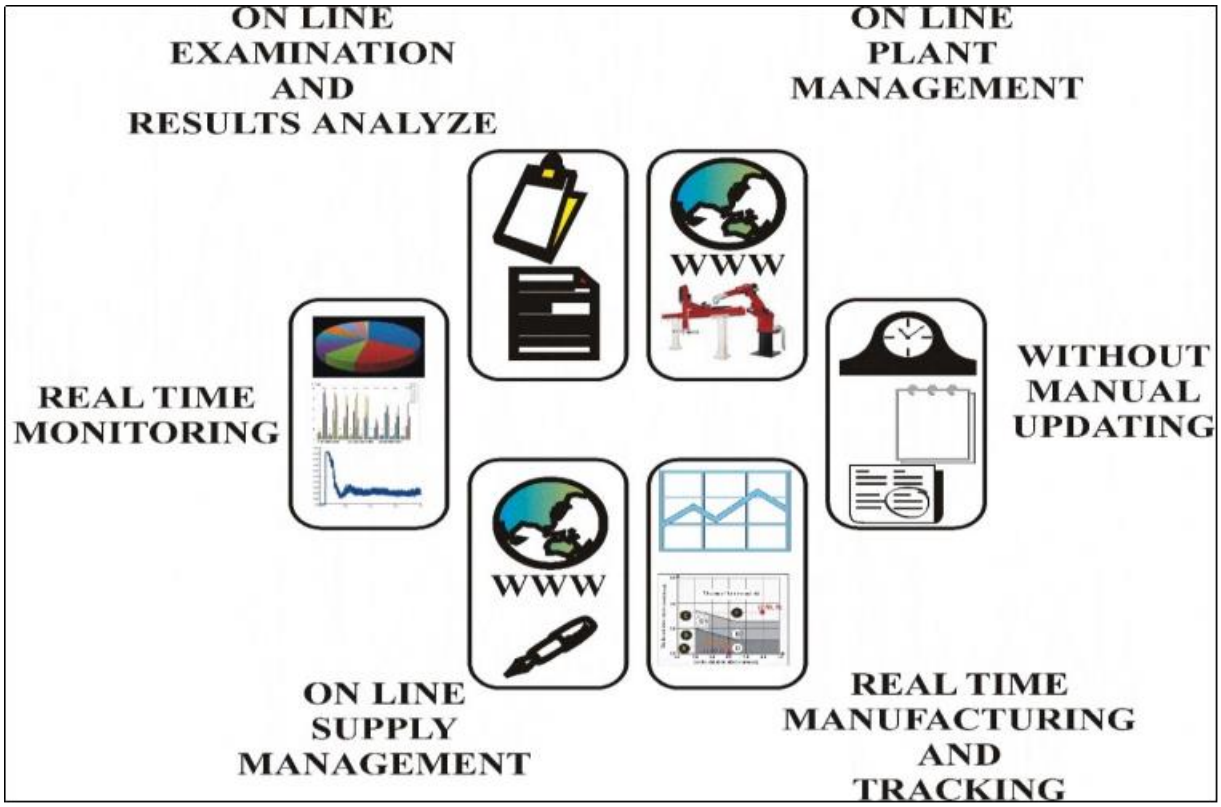

Figure 1: The main concept of Industry 4.0 in pharmaceutical industry

This system is managed with artificial intelligence techniques, principles, and methods. Production, intelligence, communication, and networking enable the appliance of Industry 4.0 in pharmacy. The main difference between the pharmacy production model and the model presented as the Industry 4.0 concept is in the transformation from automatic process control and reactive reporting about events to events prediction and their analysis through the whole supply and delivery chain. The automatic management system in the old concept determines what is wrong, while the Pharma 4.0 concept predicts what will be wrong and how to avoid it. Also, the management of production processes in pharmacy presents one of the main and most important differences. Reactive action and reporting present the features of today`s automotive processes. The process is tracked, with all of its parameters, where any kind of mistake or failure can be noticed by humans, in the sense of human reaction. Pharma 4.0 presents a completely new approach in the sense of scraps, failures, mistakes, and other bad possibilities elimination. Related to the powerful and sensitive sensor systems, huge amounts of data from any kind of process can be collected. This data can be detailed and systematically processed and as a result, the whole processes or events can be predicted. This approach enables any kind of bad effects can be prevented in advance. In the framework of automated management, production planning, production and assembly, quality assurance, and packing with logistics are tracked and monitored, where any kind of mistake can be noticed, and after that, any reaction can be realized. In the framework of Pharma 4.0, production planning, production and assembly, quality assurance, and packing with logistics can be predicted, with precise manuals and directions on how, where, and when any kind of

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mistake can be avoided. The main differences between the present model of the pharmaceutical industry and the model represented as the concept of Industry 4.0 in Pharmacy are presented in Figure 2 [2,3].

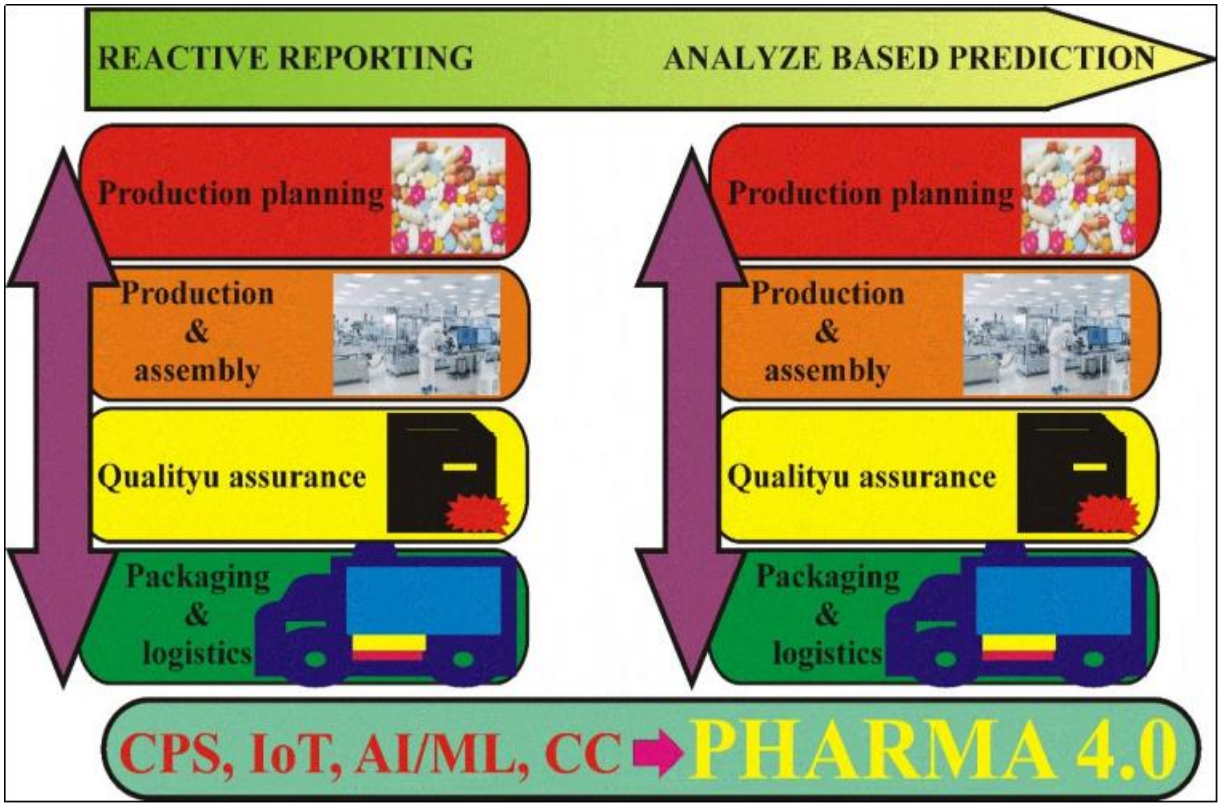

Figure 2: The main differences between today`s model of pharmaceutical production and model presented as concept of Industry 4.0 in Pharmacy

PHARMA 4.0 - Main Elements and Aims

As presented in Figure 2, the main elements of Pharma 4.0 are cyber-physical systems (CPS), the Internet of things (IoT), and cloud computing (CC) with a hard boost of machine learning (ML) and artificial intelligence (AI) techniques, principles and methods. These elements must be connected and unified in one unique system. So, one of the most important aims is the creation of, so so-called, smart pharmaceutical factory. This factory should present one intelligent manufacturing ambient, where manufacturing resources, additional, and logistic systems are organized and supervised without human assistance or action. Modern and powerful conditions of networking enable smart, developed, and profitable manufacturing. The preparation of manufacturing is arranged at a new and high level. Factory processes and procedures are analyzed, tracked, and monitored in real-time to the smallest levels and details, such as, for example, manufacturing lines, machines, robots, regulations, regular standards, etc. Generally, a smart networked factory is characterized by: online tracking and monitoring of procedures, processes, robots, machines, and similar in the sense of regulation and potential right-timed changes; smart manufacturing without scrap, garbage, or errors; a significant increase of market; significant increasing of profit; maximal elimination of jams

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and stops thanks to the help of smart maintenance and prediction; unification of all complex parameters and their tracking, monitoring, and prediction; realization of automotive operations related to analyse of huge information with complete elimination of all manual operations. Generally, these elements are presented in Figure 3.

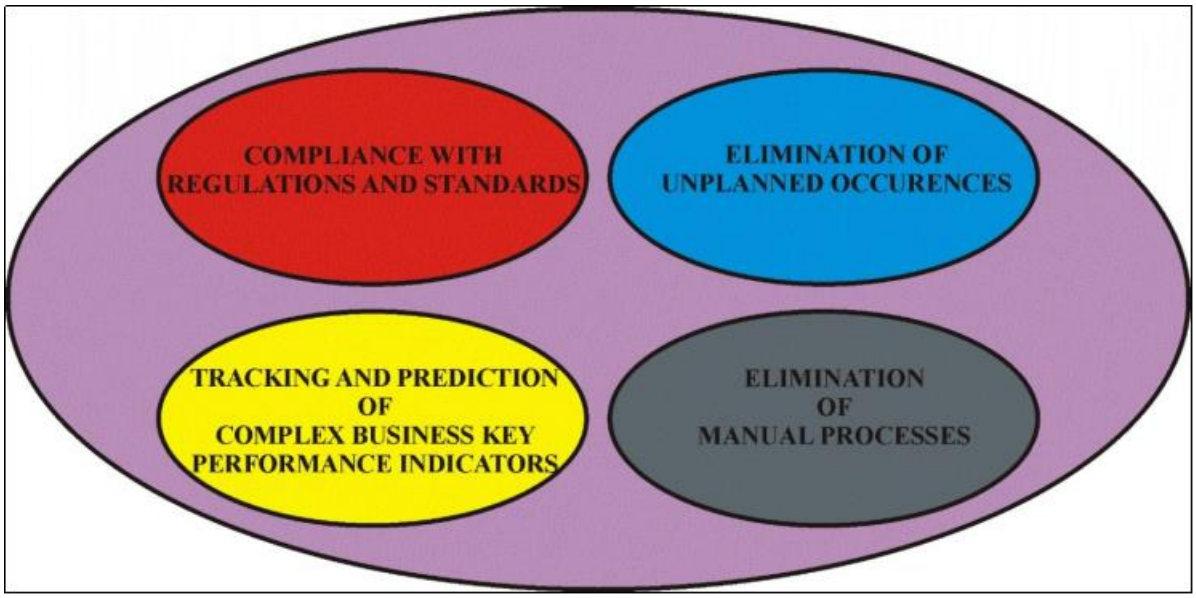

Figure 3: The most important elements of Pharma 4.0 in appliance

Compliance with regulations and standards purports tracking and monitoring with bar codes, increasing incomes, and increasing market. Design a system for tracking and predicting complex business KPIs, analyzing large amounts of data to ultimately increase income. Elimination of unplanned occurrences purports the elimination of jams, stops, in generally, all potential unwanted situations that can endanger the system functioning; predictive maintenance; management with active and passive property; increasing of incomes and costs reduction. Elimination of manual processes purports automatic activities based on predictive and reactive information and cost reduction [2,4]

Data Integrity

Data presents crucial parameters for smart manufacturing in any industrial sphere, so as in Pharmacy. Of course, data must be transformed into a concrete informational context, understandable for users. The complete period of collecting, transferring, storing, processing, analyzing, visualization, and appliance of data presents their life cycle. One of the very important problems, not only in the Pharmacy, is the data integrity. Patients' data integrity was always complex and accessible to malversation. Data are generated with huge speed, in real-time, and in different formats. Their quantities are enormous and they must have the ability to be filtered and analyzed (with proper method or algorithm appliance). Many different organizations and institutions don’t have precisely defined processes data flows and directions. Pharma 4.0 purported data transfer in all directions with complete transparency and clear process flow related to data. Data integrity is very complex and purports not only the precise traceability of organization processes but also appropriate data quality, adequate data contents, and acceptance of the ALCOA (attributable, legible, contemporaneous,

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original, accurate) principle. The processes must be precisely organized, defined, and flexible. Data integrity also demands strong and precise risk management with a strong critical opinion. An effective and flexible manufacturing system with all of the accompanying components and elements demands strong data flow with huge data availability but at the same time strong potential for data protection. Data are transferred continually between different information systems, cyber-physical systems, and their users. Also, data storage presents a very important and always actual problem; for example, during the life cycle of the process, related data can increase significantly. Today, with the use of cloud computing (CC), it is possible to store enormous amounts of data in a payable, flexible, highly available, and effective way. Huge amounts of data, generated from different sources, their understanding and manipulation in consultation with knowledge and experience present the most important thing in optimal decision realization. Through data analysis, related to understanding of developed model, designers can „translate "different customers' demands into production characteristics and quality characteristics [5, 6].

Quality Management in Pharma 4.0

Related to the known facts, today`s quality management strategy in pharmacy is based on the management of the individual processes that are key to providing the most important conditions and characteristics for the quality of the product and the realization of the designed quality of the product.

This purports the strengthening of supply chain systems (SSCC) and strong control of quality (critical quality attribute CQA). This approach has good sides and advantages, but it also lacks. One of the most important lacks is the impossibility of management for different activities and occurrences with huge importance for so-called processes dissipation. Many processes have a lot of characteristics and parameters with a lot of known unknown and unpredictable variations that can be of great importance to production flow and production quality. These variations are numerous and hard to select and determine but also hard to predict (different disturbances; the presence of different impurities, obstacles, obstructions, perturbations, and similar; different influences, etc.). Many of them can be embedded in the material, function, process, or/and they can occur during the entire life cycle of the product. These variations are not the subject of consideration for the strengthening supply chain system. It is obvious that the strategy of quality management, arising from product development, must be improved in the sense of appliance in manufacturing.

Quality management in Pharma 4.0 was based on the ICH Q10 (The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use) model. In this model, the pharmaceutical quality system was integrated with four important elements: resources, information system, system of processes, and cultures. This unified model was called as holistic model ICH Q10 for Pharma 4.0. The manager`s responsibility, in the form of ICH Q10, purports tracking, analyzing, and proper reaction at every phase: pharmaceutical development, technology transfer, commercial production, and eventual production stoppage. Through the performance of processes and system of production quality tracking, elements or parts of pharmacy quality scheme such as corrective action, a system of preventive actions, management of changes, and management review are transformed in the qualified and available manpower, the integrated net of holistic values, management of holistic strategy in the lifecycle of the product and modern solutions of the communication and decision making [7]. New elements were made available by digitalization. The noted model combines the

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production quality management strategy and production quality control strategy related to the whole lifecycle of the product. With data integrity, the holistic strategy of quality control for the complete lifecycle of the product was formed. Related to this model, important parameters were defined: critical quality attributes (CQA), critical parameters of the processes (CPP), and important material characteristics (CMA). These noted parameters are the most important parameters for a product`s design. On the other side, ICH Q12 identified noted parameters as established conditions to be followed by pharmaceutical quality systems and processes performance. The so-called „model of established conditions (EC)“ is presented in Figure 4.

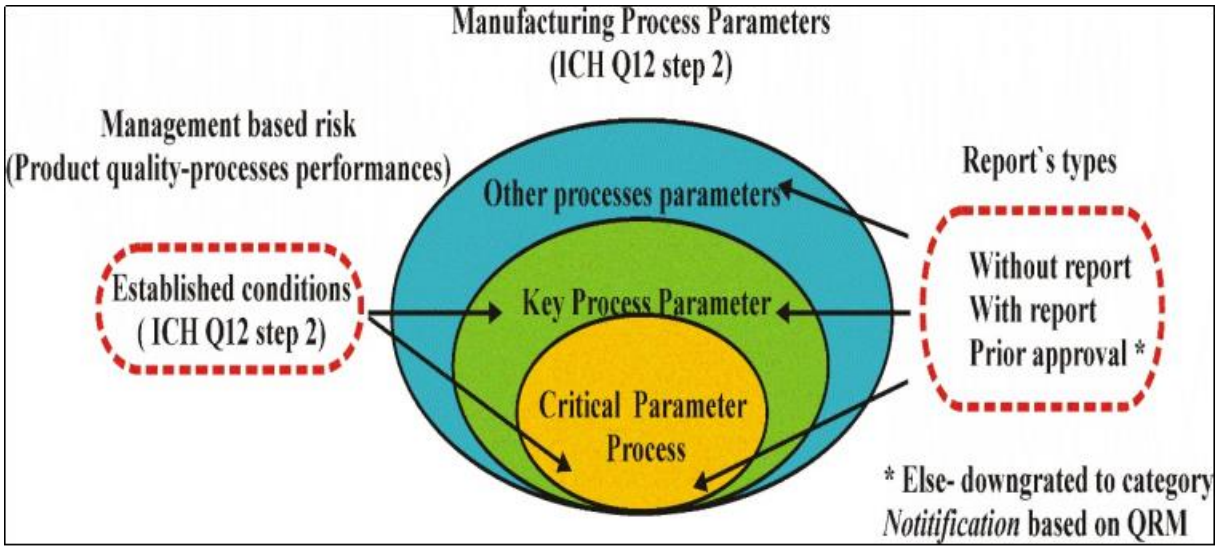

Figure 4: The model of established conditions (EC)

In the management sense, the holistic concept of the pharmacy provides integration of all included models, processes, parts, units, and other elements with information technologies. In that way, decision-making is significantly increased, with information integrity and needed analyses. Also, the appliance of holistic strategy in the pharmaceutical industry in the sense of realization and accommodation with valid regulations and rules presents the crucial factor for the lifecycle management of pharmaceutical products, an adequate approach based on risk, and precisely defined business and pharmaceutical processes [8,9].

Conclusion

It is an obvious fact that Industry 4.0 has been involved in pharmacy and created one new model and concept - Pharma 4.0. This model was defined from Industry 4.0 through the special operative model for pharmaceutical productions. Of course, it purported involving and use of the best examples related to health regulations; designing of totally new connections between industry, law and regulations, healthcare, production, organization, a new level of cultural cooperation, and all other important elements. The benefits of the appliance of Pharma 4.0 are numerous and huge, as it was noted in the previous text. It is a fact that the level of Pharma 4.0 is not the same, from country to country and it demands digital maturity and compliance between key elements, but also the prerequisite that pharmacy quality schemes and controlled manufacturing systems, processes, and products are

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established. That new level purports and provides a holistic approach for designing and management procedures, processes, business and manufacturing units, and other important elements and parameters important for manufacturing process, production, and quality.

As the lack of Pharma 4.0, the business risk and staff employment were noted as real and sensitive things. Generally, staff employment presents a potential future problem for the whole of Industry 4.0. Related to many studies, many professions will disappear or they will be changed with robots, machines, and artificial intelligence. So, it is of course a present and future „burning "problem that must be solved continuously and rationally [10].

It is also important to note that many studies consider that Pharma 4.0 is not necessary and that presents a concurrent advantage, related to digitalization, which is necessary.

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